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(54) Title: MEMBRANE–BOUND PROTEINS AND NUCLEIC ACIDS ENCODING THE SAME

(57) Abstract

The present invention is directed to polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

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NOVEL POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

FIELD OF THE INVENTION

The present invention relates generally to the identification and isolation of novel DNA and to the recombinant production of novel polypeptides.

BACKGROUND OF THE INVENTION

Extracellular proteins play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

Secreted proteins have various industrial applications, including as pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents. Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci. 93:7108-7113 (1996); U.S. Patent No. 5,536,637)].

Membrane-bound proteins and receptors can play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesin molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interactions. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are being undertaken by both industry and academia to identify new, native receptor or membrane-bound proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor or membrane-bound proteins.

1. **PRO281**

A novel gene designated testis enhanced gene transcript (TEGT) has recently been identified in humans (Walter et al., Genomics 20:301-304 (1995)). Recent results have shown that TEGT protein is developmentally regulated in the mammalian testis and possesses a nuclear targeting motif that allows the protein to localize to the nucleus (Walter et al., Mamm. Genome 5:216-221 (1994)). As such, it is believed that the TEGT protein plays an important role in testis development. There is, therefore, substantial interest in identifying and characterizing novel polypeptides having homology to the TEGT protein. We herein describe the identification and characterization of novel polypeptides having homology to TEGT protein, designated herein as PRO281 polypeptides.

2. **PRO276**

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO276 polypeptides.

3. **PRO189**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO189 polypeptides.

4. **PRO190**

Of particular interest are proteins having seven transmembrane domains (7TM), or more generally, all multiple transmembrane spanning proteins. Among multiple transmembrane spanning proteins are ion channels and transporters. Examples of transporters are the UDP-galactose transporter described in Ishida, et al., J. Biochem., 120(6):1074-1078 (1996), and the CMP-sialic acid transporter described in Eckhardt, et al., PNAS, 93(15):7572-7576 (1996). We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO190 polypeptides.

5. PRO341

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO341 polypeptides.

6. PRO180

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO180 polypeptides.

7. PRO194

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO194 polypeptides.

8. PRO203

Enzymatic proteins play important roles in the chemical reactions involved in the digestion of foods, the biosynthesis of macromolecules, the controlled release and utilization of chemical energy, and other processes necessary to sustain life. ATPases are a family of enzymes that play a variety of important roles, including energizing transport of ions and molecules, across cellular membranes. Transport mechanisms that employ ATPases often involve excluding xeno- and endobiotic toxins from the cellular environment, thereby protecting cells from toxicity of these compounds. Lu et al. report a detoxification mechanism where glutathione S-transferase (GST) catalyzes glutathionation of plant toxins, and a specific Mg^{2+} -ATPase is involved in the transport of the glutathione S-conjugates from the cytosol. Proc. Natl. Acad. Sci. USA 94(15):8243-8248 (1997). This study and others indicate the importance of the identification of ATPases, such as GST ATPases, and of novel proteins having sequence identity with ATPases.

More generally, and also of interest are novel membrane-bound proteins, including those which may be involved in the transport of ions and molecules across membranes. Membrane-bound proteins and receptors can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell

interactions, and cellular adhesin molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

In light of the important physiological roles played by ATPases and membrane-bound proteins efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins, and proteins having sequence identity to ATPases. We herein describe the identification and characterization of novel polypeptides having sequence identity to GST ATPase, designated herein as PRO203 polypeptides.

9. PRO290

Of particular interest are novel proteins and nucleic acids which have sequence identity with known proteins and nucleic acids. Proteins of interest which are well known in the art include NTII-1, a nerve protein which facilitates regeneration, FAN, and beige. Beige, or bg, is a murine analog related to Chediak-Higashi Syndrome (CHS), a rare autosomal recessive disease in which neutrophils, monocytes and lymphocytes contain giant cytoplasmic granules. See Perou et al., J. Biol. Chem. 272(47):29790 (1997) and Barbosa et al., Nature 382:262 (1996).

We herein describe the identificationand characterization of novel polypeptides having sequence identity to NTII-1, FAN and beige, designated herein as PRO290 polypeptides.

10. PRO874

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO194 polypeptides.

11. PRO710

In *Saccharomyces cerevisiae*, the chromatin structure of DNA replication origins changes as cells become competent for DNA replication, suggesting that G1 phase-specific association of replication factors with origin DNA regulates entry into S phase (Aparicio et al., Cell 91:59-69 (1997)). In fact, it has been shown that the initiation of DNA replication in Saccharomyces cerevisiae requires the protein product of the CDC45 gene which encodes a protein that stays at relatively constant levels throughout the cell cycle (Owens et al., Proc. Natl. Acad. Sci USA 94:12521-12526 (1997)). The CDC45 protein is part of a prereplication complex that may move with DNA replication forks in yeast. Given the obvious importance of the CDC45 protein in DNA replication, there is significant interest in identifying and characterizing novel polypeptides having homology to CDC45. We herein describe the identification and characterization of novel polypeptides having homology to the CDC45 protein, designated herein as PRO710 polypeptides.

12. PRO1151

The complement proteins comprise a large group of serum proteins some of which act in an enzymatic cascade, producing effector molecules involved in inflammation. The complement proteins are of particular importance in regulating movement and function of cells involved in inflammation. One of the complement proteins, C1q, has been shown to be involved in the recognition of microbial surfaces and antibody-antigen complexes in the classical pathway of complement (Shapiro et al., Curr. Biol. 8(6):335-338 (1998)).

Given the physiological importance of inflammation and related mechanisms *in vivo* and in the specific physiological activities of complement C1q protein, efforts are currently being undertaken to identify new, native proteins which share sequence similarity to the complement proteins. We herein describe the identification and characterization of novel polypeptides having homology to complement C1q protein, designated herein as PRO1151 polypeptides.

13. PRO1282

All proteins containing leucine-rich repeats are thought to be involved in protein-protein interactions. Leucine-rich repeats are short sequence motifs present in a number of proteins with diverse functions and cellular locations. The crystal structure of ribonuclease inhibitor protein has revealed that leucine-rich repeats correspond to beta-alpha structural units. These units are arranged so that they form a parallel beta-sheet with one surface exposed to solvent, so that the protein acquires an unusual, nonglubular shape. These two features have been indicated as responsible for the protein-binding functions of proteins containing leucine-rich repeats. See, Kobe and Deisenhofer, Trends Biochem. Sci., 19(10):415-421 (Oct. 1994); Kobe and Deisenhofer, Curr. Opin. Struct. Biol., 5(3):409-416 (1995).

A study has been reported on leucine-rich proteoglycans which serve as tissue organizers, orienting and ordering collagen fibrils during ontogeny and are involved in pathological processes such as wound healing, tissue repair, and tumor stroma formation. Iozzo, R. V., Crit. Rev. Biochem. Mol. Biol., 32(2):141-174 (1997). Others studies implicating leucine rich proteins in wound healing and tissue repair are De La Salle, C., et al., Vouv. Rev. Fr. Hematol. (Germany), 37(4):215-222 (1995), reporting mutations in the leucine rich motif in a complex associated with the bleeding disorder Bernard-Soulier syndrome, Chlemetson, K. J., Thromb. Haemost. (Germany), 74(1):111-116 (July 1995), reporting that platelets have leucine rich repeats and Ruoslahti, E. I., et al., WO9110727-A by La Jolla Cancer Research Foundation reporting that decorin binding to transforming growth factorβ has involvement in a treatment for cancer, wound healing and scarring. Related by function to this group of proteins is the insulin like growth factor (IGF), in that it is useful in wound-healing and associated therapies concerned with re-growth of tissue, such as connective tissue, skin and bone; in promoting body growth in humans and animals; and in stimulating other growth-related processes. The acid labile subunit of IGF (ALS) is also of interest in that it increases the half-life of IGF and is part of the IGF complex *in vivo*.

Another protein which has been reported to have leucine-rich repeats is the SLIT protein which has been reported to be useful in treating neuro-degenerative diseases such as Alzheimer's disease, nerve damage such as in Parkinson's disease, and for diagnosis of cancer, see, Artavanistsakonas, S. and Rothberg, J. M., WO9210518-A1 by Yale University. Of particular interest is LIG-1, a membrane glycoprotein that is expressed

specifically in glial cells in the mouse brain, and has leucine rich repeats and immunoglobulin-like domains. Suzuki, et al., J. Biol. Chem. (U.S.), 271(37):22522 (1996). Other studies reporting on the biological functions of proteins having leucine rich repeats include: Tayar, N., et al., Mol. Cell Endocrinol., (Ireland), 125(1-2):65-70 (Dec. 1996) (gonadotropin receptor involvement); Miura, Y., et al., Nippon Rinsho (Japan), 54(7):1784-1789 (July 1996) (apoptosis involvement); Harris, P. C., et al., J. Am. Soc. Nephrol., 6(4):1125-1133 (Oct. 1995) (kidney disease involvement).

Leucine rich repeat proteins are further discussed in Kajava, J. Mol. Biol., 277(3):519-527 (1998), Nagasawa, et al., Genomics, 44(3):273-279 (1997), Bengtsson, J. Biol. Chem., 270(43):25639-25644 (1995), Gaillard, et al., Cell, 65(7):1127-1141 (1991) and Ohkura and Yanagida, Cell, 64(1):149-157 (1991), all incorporated herein by reference.

Thus, due to all the reasons listed above, new members of the leucine rich repeat superfamily are of interest. On a more general level, all novel proteins are of interest. We herein describe the identification and characterization of novel leucine-rich repeat-containing polypeptides, designated herein as PRO1282 polypeptides.

14. **PRO358**

The cloning of the Toll gene of *Drosophila*, a maternal effect gene that plays a central role in the establishment of the embryonic dorsal-ventral pattern, has been reported by Hashimoto et al., Cell 52:269-279 (1988). The *Drosophila* Toll gene encodes an integral membrane protein with an extracytoplasmic domain of 803 amino acids and a cytoplasmic domain of 269 amino acids. The extracytoplasmic domain has a potential membrane-spanning segment, and contains multiple copies of a leucine-rich segment, a structural motif found in many transmembrane proteins. The Toll protein controls dorsal-ventral patterning in *Drosophila* embryos and activates the transcription factor Dorsal upon binding to its ligand Spätzle. (Morisato and Anderson, Cell 76:677-688 (1994)). In adult *Drosophila*, the Toll/Dorsal signaling pathway participates in the anti-fungal immune response. (Lenaitre et al., Cell 86:973-983 (1996)).

A human homologue of the *Drosophila* Toll protein has been described by Medzhitov et al., Nature 388:394-397 (1997). This human Toll, just as *Drosophila* Toll, is a type I transmembrane protein, with an extracellular domain consisting of 21 tandemly repeated leucine-rich motifs (leucine-rich region - LRR), separated by a non-LRR region, and a cytoplasmic domain homologous to the cytoplasmic domain of the human interleukin-1 (IL-1) receptor. A constitutively active mutant of the human Toll transfected into human cell lines was shown to be able to induce the activation of NF-κB and the expression of NF-κB-controlled genes for the inflammatory cytokines IL-1, IL-6 and IL-8, as well as the expression of the constimulatory molecule B7.1, which is required for the activation of native T cells. It has been suggested that Toll functions in vertebrates as a non-clonal receptor of the immune system, which can induce signals for activating both an innate and an adaptive immune response in vertebrates. The human Toll gene reported by Medzhitov et al., *supra* was most strongly expressed in spleen and peripheral blood leukocytes (PBL), and the authors suggested that its expression in other tissues may be due to the presence of macrophages and dendritic cells, in which it could act as an early-warning system for infection. The public GenBank database contains the following Toll sequences: Toll1

(DNAX# HSU88540-1, which is identical with the random sequenced full-length cDNA #HUMRSC786-1); Toll2 (DNAX# HSU88878-1); Toll3 (DNAX# HSU88879-1); and Toll4 (DNAX# HSU88880-1, which is identical with the DNA sequence reported by Medzhitov et al., *supra*). A partial Toll sequence (Toll5) is available from GenBank under DNAX# HSU88881-1.

Further human homologues of the Drosophila Toll protein, designated as Toll-like receptors (huTLRs1-5) were recently cloned and shown to mirror the topographic structure of the Drosophila counterpart (Rock et al., Proc. Natl. Acad. Sci. USA 95:588-593 [1998]). Overexpression of a constitutively active mutant of one human TLR (Toll-protein homologue - Medzhitov et al., *supra*; TLR4 - Rock et al., *supra*) leads to the activation of NF-κB and induction of the inflammatory cytokines and constimulatory molecules. Medzhitov et al., *supra*.

We herein describe the identification and characterization of novel polypeptides having homology to Toll, designated herein as PRO358 polypeptides.

15. **PRO1310**

Of interest are proteins related to carboxypeptidases. Various carboxypeptidases are described in the literature, i.e., Krause et al., Immunol. Rev. 161:119-127 (1998) and Leiter, J. Endocrinol. 155(2):211-214 (1997). We herein describe the identification and characterization of novel polypeptides having homology to a carboxypeptidase, designated herein as PRO1310 polypeptides.

16. **PRO698**

The extracellular mucous matrix of olfactory neuroepithelium is a highly organized structure in intimate contact with chemosensory cilia that house the olfactory transduction machinery. The major protein component of this extracellular matrix is olfactomedin, a glycoprotein that is expressed in olfactory neuroepithelium and which form intermolecular disulfide bonds so as to produce a polymer (Yokoe et al., Proc. Natl. Acad. Sci. USA 90:4655-4659 (1993), Bal et al., Biochemistry 32:1047-1053 (1993) and Snyder et al., Biochemistry 30:9143-9153 (1991)). It has been suggested that olfactomedin may influence the maintenance, growth or differentiation of chemosensory cilia on the apical dendrites of olfactory neurons. Given this important role, there is significant interest in identifying and characterizing novel polypeptides having homology to olfactomedin. We herein describe the identification and characterization of novel polypeptides having homology to olfactomedin protein, designated herein as PRO698 polypeptides.

17. **PRO732**

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides having sequence identity to the Diff33 protein, designated herein as PRO732 polypeptides.

18. **PRO1120**

Enzymatic proteins play important roles in the chemical reactions involved in the digestion of foods, the biosynthesis of macromolecules, the controlled release and utilization of chemical energy, and other processes necessary to sustain life. Sulfatases are a family of secreted enzymatic proteins that play a variety of important metabolic roles and thus are the subject of interest in research and industry (see, e.g., Sleat et al., Biochem J., 324(Pt. 1):33-39 (1997)). Deficiencies of certain sulfatases have been implicated in various human disorders including Sanfilippo D syndrome (see, Litjens et al., Biochem J. 327(Pt 1):899-94 (1997); Leipprandt et al. J. Inherit Metab. Dis. 18(5):647-648 (1995); and Freeman et al. Biochem J. 282(pt2):605-614 (1992)). We herein describe the identification and characterization of novel polypeptides having sequence identity to sulfatase protein, designated herein as PRO1120 polypeptides.

19. **PRO537**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO537 polypeptides.

20. **PRO536**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO536 polypeptides.

21. **PRO535**

Isomerase proteins play many important physiological roles in the mammal. Many different types of isomerase proteins have been identified and characterized including, for example, protein disulfide isomerases and peptidyl-prolyl isomerases. It has been reported that many immunophilin proteins, i.e., proteins that serves as receptors for immunosuppressant drugs, exhibit peptidyl-prolyl isomerase activity in that they function to catalyze the interconversion of the cis and trans isomerase of peptide and protein substrates for immunophilin proteins. As such, there is significant interest in identifying and characterizing novel polypeptides having sequence similarity to peptidyl-prolyl isomerase proteins. We herein describe the identification and characterization of novel polypeptides having homology to a putative peptidyl-prolyl isomerase protein, designated herein as PRO535 polypeptides.

22. **PRO718**

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and

characterization of novel transmembrane polypeptides, designated herein as PRO718 polypeptides.

23. PRO872

Enzymatic proteins play important roles in the chemical reactions involved in the digestion of foods, the biosynthesis of macromolecules, the controlled release and utilization of chemical energy, and other processes necessary to sustain life. Dehydrogenases and desaturases are a family of enzymes that play a variety of important metabolic roles and thus are the subject of interest in research and industry (see Hable et al., Mol. Gen. Genet. 257(2):167-176 (1998); Schneider, C. et al., Prot. Expr. Purif. 10(2): 175-179 (1997)). We herein describe the identification and characterization of novel polypeptides having sequence identity to dehydrogenase proteins, designated herein as PRO872 polypeptides.

24. PRO1063

Collagens constitute the most abundant proteins of the extracellular matrix (ECM) in mammalian organisms. Collagen and other macromolecules of the ECM are deposited by resident cells and organized into a three-dimensional meshwork. This ECM environment plays an essential role in guiding cell migration and in cell-to-cell communication during morphogenic processes. The restructuring of the ECM during remodeling occurs as a cooperative multistep process involving a localized degradation of existing macromolecules, rearrangement of the cytoskeleton, cell translocation, and deposition of new ECM components. Involved in this restructuring are enzymes such as collagenases and gelatinases which play important roles in the degradation of the ECM. In light of the obviously important roles played by the collagenase enzymes, there is substantial interest in identifying and characterizing novel polypeptides having homology to these proteins. We herein describe the identification and characterization of novel polypeptides having homology to human type IV collagenase protein, designated herein as PRO1063 polypeptides.

25. PRO619

Immunoglobulins are antibody molecules, the proteins that function both as receptors for antigen on the B-cell membrane and as the secreted products of the plasma cell. Like all antibody molecules, immunoglobulins perform two major functions: they bind specifically to an antigen and they participate in a limited number of biological effector functions. Therefore, new members of the Ig superfamily are always of interest.

Of particular interest are novel gene products associated with mu chains in immature B cells. Shirasawa, et al., EMBO J., 12(5):1827-1834 (1993); Dul, et al., Eur. J. Immunol., 26(4):906-913 (1996). Moreover, the molecular components and assembly of mu surrogate light chain complexes in pre-B cell lines are of interest. Ohnishi and Takemori, J. Biol. Chem., 269(45):28347-28353 (1994); Bauer, et al., Curr. Top. Microbiol., 137:130-135 (1988). Novel nucleic acids and peptides related to VpreB1, VpreB2 and VpreB3 by sequence identity are of particular interest. The assembly and manipulation of immunoglobulins can effect the entire industry related to antibodies and vaccines.

We herein describe the identification and characterization of novel polypeptides having homology to VpreB proteins, designated herein as PRO619 polypeptides.

26. PRO943

Fibroblast growth factor (FGF) proteins exhibit a variety of activities and act by binding to cell surface fibroblast growth factor receptors. Many different fibroblast growth factor receptors have been identified and characterized, including the fibroblast growth factor receptor-4, which has been shown to be a high affinity receptor for both acidic and basic FGF (Ron et al., J. Biol. Chem. 268:5388-5394 (1993) and Stark et al., Development 113:641-651 (1991)). Given the obvious importance of the FGF family of proteins and the cell surface receptors to which they bind, there is significant interest in identifying novel polypeptides having homology to the FGF receptor family. We herein describe the identification and characterization of novel polypeptides having homology to the fibroblast growth factor receptor-4 protein, designated herein as PRO943 polypeptides.

27. PRO1188

The identification of nucleotide pyrophosphohydrolases has been of interest because of the potential roles these secreted molecules play in calcium pyrophosphate dihydrate (CPPD) deposition disease, arthritis, and other joint diseases (see Masuda et al. J. Rheumatol. (997) 24(8):1588-1594; and Terkeltaub et al., Arthritis Rheum (1998) 37(6):934-941). We herein describe the identification and characterization of novel polypeptides having homology to nucleotide pyrophosphohydrolases, designated herein as PRO1188 polypeptides.

28. PRO1133

Netrins are molecules that guide growing axons and that are strikingly similar in sequence and in function in flies, nematodes and vertebrates. Additionally, netrin receptors have been identified in all three animal groups and shown to have crucial, conserved roles in axon navigation. Netrins and their receptors are further described in the literature, i.e., Varela-Echavarria and Guthrie, Genes Dev., 11(5):545-557 (1997); Guthrie, Curr. Biol., 7(1):R6-R9 (1997); and Keynes and Cook, Neuron, 17(6):1031-1034 (1996). Due to their relation to neurons, netrins and their related proteins are of interest. Of particular interest are molecules having sequence identity or similarity with netrin. We herein describe the identification and characterization of novel polypeptides having homology to netrins, designated herein as PRO1133 polypeptides.

29. PRO784

Of interest are membrane-bound and receptor proteins involved in intracellular signaling, metabolism, transport, and other pathways. For example, membrane-bound proteins of the endoplasmic reticulum and golgi apparatus play important roles in the transport of proteins. The sec22 protein is an endoplasmic reticulum membrane-bound protein involved in fundamental membrane trafficking reactions where secretory products are routed from their site of synthesis to their final destination. The roles of sec22 in transport pathways have been reported by numerous investigators (see Tang et al., Biochem Biophys Res Commun 243(3):885-891 (1998); Hay et al., J. Biol. Chem. 271(10):5671-5679 (1996); and Newman et al., Mol. Cell. Biol. 10(7):3405-3414 (1990)). We herein describe the identification and characterization of novel polypeptides having homology to sec22, designated herein as PRO784 polypeptides.

30. **PRO783**

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO783 polypeptides.

31. **PRO820**

Immunoglobulin molecules play roles in many important mammalian physiological processes. The structure of immunoglobulin molecules has been extensively studied and it has been well documented that intact immunoglobulins possess distinct domains, one of which is the constant domain or F_c region of the immunoglobulin molecule. The F_c domain of an immunoglobulin, while not being directly involved in antigen recognition and binding, does mediate the ability of the immunoglobulin molecule, either uncomplexed or complexed with its respective antigen, to bind to F_c receptors either circulating in the serum or on the surface of cells. The ability of an F_c domain of an immunoglobulin to bind to an F_c receptor molecule results in a variety of important activities, including for example, in mounting an immune response against unwanted foreign particles. Thus, molecules related to F_c receptors are of interest. F_c receptors are further described in Tominaga et al., Biochem. Biophys. Res. Commun., 168(2):683-689 (1990); Zhang et al., Immuno., 39(6):423-427 (1994). We herein describe the identification and characterization of novel polypeptides having homology to F_c receptor, designated herein as PRO820 polypeptides.

32. **PRO1080**

The folding of proteins and the assembly of protein complexes within subcompartments of the eukaryotic cell is catalysed by different members of the Hsp70 protein family. The chaperone function of Hsp70 proteins in these events is regulated by members of the DnaJ-like protein family, which occurs through direct interaction of different Hsp70 and DnaJ-like protein pairs that appear to be specifically adapted to each other. The diversity of functions of DnaJ-like proteins using specific examples of DnaJ-Hsp70 interactions with polypeptides in yeast protein-biogenesis pathways is further described in Cyr et al., Trends Biochem. Sci., 19(4):176-181 (1994). DnaJ proteins and their involvement in the binding of secretory precursor polypeptides to a translocon subcomplex and polypeptide translocation machinery in the yeast endoplasmic reticulum are further described in Lyman and Schekman, Cell 88(1):85-96 (1997) and Lyman and Schekman, Experientia 52(12):1042-1049 (1996), respectively. Thus, DnaJ proteins are of interest, as are proteins related to DnaJ proteins, particularly those having sequence identity with DnaJ proteins. We herein describe the identification and characterization of novel polypeptides having homology to DnaJ proteins, designated herein as PRO1080 polypeptides.

33. **PRO1079**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel

secreted polypeptides, designated herein as PRO1079 polypeptides.

34. **PRO793**

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO793 polypeptides.

35. **PRO1016**

Enzymatic proteins play important roles in the chemical reactions involved in the digestion of foods, the biosynthesis of macromolecules, the controlled release and utilization of chemical energy, and other processes necessary to sustain life. Acyltransferases are enzymes which acylate moieties. Acyl-glycerol-phosphate acyltransferases can act on lysophosphatidic acid as a substrate. The lysophosphatidic acid is converted to phophatidic acid and thus plays a role in forming phosphatidylethanolamine found in membranes. See, Brown, et al., Plant Mol. Biol., 26(1):211-223 (1994). Thus, acyltransferases play an important role in the biosynthesis of molecules requiring acylation. We herein describe the identification and characterization of novel polypeptides having homology to acyltransferase proteins, designated herein as PRO1016 polypeptides.

36. **PRO1013**

Efforts are being undertaken by both industry and academia to identify new, native proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel proteins. We herein describe the identification and characterization of novel polypeptides, designated herein as PRO1013 polypeptides.

37. **PRO937**

The glypican family of heparan sulfate proteoglycans are major cell-surface proteoglycans of the developing nervous system. It is believed that members of the glypican family play a role in regulating cell cycle progression during the transition of proliferating neuronal progenitor cells to differentiated neurons. Lander et al. Perspect Dev. Neurobiol 3(4):347-358 (1996). It is likely that proteoglycans of the glypican family play other important roles in neural development (Lander et al., *supra*), and as well as other tissues, as glypican family members have also been found in the developing kidney (Watanabe et al. J. Cell Biol. 130(5):1207-1218 (1995)). Accordingly, the identification of new members of the glypican family of proteins is of interest in research and in industry.

Described herein is the identificationand characterization of novel polypeptides having sequence identity with glypican family proteins, designated herein as PRO937 polypeptides.

38. **PRO842**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO842 polypeptides.

39. **PRO839**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO839 polypeptides.

40. **PRO1180**

Methyltransferase enzymes catalyze the transfer of methyl groups from a donor molecule to an acceptor molecule Methyltransferase enzymes play extremely important roles in a number of different biological processes including, for example, in the electron transport chain in the plasma membrane in prokaryotes and in the inner mitochondrial membrane in eukaryotic cells (see, e.g., Barkovich et al., J. Biol. Chem. 272:9182-9188 (1997), Dibrov et al., J. Biol. Chem. 272:9175-9181 (1997), Lee et al., J. Bacteriol.. 179:1748-1754 (1997) and Marbois et al., Arch. Biochem. Biophys. 313:83-88 (1994)). Methyltransferase enzymes have been shown to be essential for the biosynthesis of ubiquinone (coenzyme Q) and menaquinone (vitamin K2), both of which are essential isoprenoid quinone components of the respiratory electron transport chain. Given the obvious importance of the methyltransferase enzymes, there is substantial interest in identifying novel polypeptide homologs of the methyltransferases. We herein describe the identification and characterization of a novel polypeptide having homology to methyltransferase enzymes, designated herein as PRO1180 polypeptides..

41. **PRO1134**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1134 polypeptides.

42. **PRO830**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO830 polypeptides.

43. **PRO1115**

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO1 115 polypeptides.

44. **PRO1277**

Efforts are being undertaken by both industry and academia to identify new, native proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor and other proteins. Of interest is the identification of proteins that may play roles in various human disorders and dysfunction. For example, the identification of proteins of the ear and the functions they play in hearing may lead to an understanding of the causes of hearing loss and deafness. Coch-B2 is one such protein that has been found to be specifically expressed in the inner ear (cochlea). It has been characterized and studied for its possible role in hearing loss (Robertson et al. Genomics (1994) 23(1):52-50; Robertson et al. Genomics (1997) 46(3):345-354). We herein describe the identification and characterization of novel polypeptides having sequence identity to Coch-B2, designated herein as PRO1277 polypeptides.

45. **PRO1135**

Glycosylation is an important mechanism for modulating the physiochemical and biological properties of proteins in a stage- and tissue-specific manner. One of the important enzymes involved in glycosylation in Saccharomyces cerevisiae is alpha 1,2-mannosidase, an enzyme that catalyzes the conversion of Man9GlcNAc2 to Man8GlcNAc2 during the formation of N-linked oligosaccharides. The Saccharomyces cerevisiae alpha 1,2-mannosidase enzyme of is a member of the Class I alpha 1,2-mannosidases that are conserved from yeast to mammals. Given the important roles played by the alpha 1,2-mannosidases in glycosylation and the physiochemical activity regulated by glycosylation, there is significant interest in identifying novel polypeptides having homology to one or more mannosidases. We herein describe the identification and characterization of novel polypeptides having homology to alpha 1,2-mannosidase protein, designated herein as PRO1135 polypeptides.

46. **PRO1114**

Interferons (IFNs) encompass a large family of secreted proteins occurring in vertebrates. Although they were originally named for their antiviral activity, growing evidence supports a critical role for IFNs in cell growth and differentiation (Jaramillo et al., Cancer Investigation 13(3):327-338 (1995)). IFNs belong to a class of negative growth factors having the ability to inhibit the growth of a wide variety of cells with both normal and transformed phenotypes. IFN therapy has been shown to be beneficial in the treatment of human malignancies such as Karposi's sarcoma, chronic myelogenous leukemia, non-Hodgkin's lymphoma, and hairy cell leukemia as well as in the treatment of infectious diseases such as hepatitis B (Gamliel et al., Scanning Microscopy 2(1):485-492 (1988), Einhorn et al., Med. Oncol. & Tumor Pharmacother. 10:25-29 (1993), Ringenberg et al.,

Missouri Medicine 85(1):21-26 (1988), Saracco et al., Journal of Gastroenterology and Hepatology 10:668-673 (1995), Gonzalez-Mateos et al., Hepato-Gastroenterology 42:893-899 (1995) and Malaguarnera et al., Pharmacotherapy 17(5):998-1005 (1997)).

Interferons can be classified into two major groups based upon their primary sequence. Type I interferons, IFN-α and IFN-β, are encoded by a superfamily of intronless genes consisting of the IFN-α gene family and a single IFN-β gene that are thought to have arisen from a common ancestral gene. Type I interferons may be produced by most cell types. Type II IFN, or IFN-γ, is restricted to lymphocytes (T cells and natural killer cells) and is stimulated by nonspecific T cell activators or specific antigens *in vivo*.

Although both type I and type II IFNs produce similar antiviral and antiproliferative effects, they act on distinct cell surface receptors, wherein the binding is generally species specific (Langer et al., Immunol. Today 9:393-400 (1988)). Both IFN-α and IFN-β bind competitively to the same high affinity type I receptor, whereas IFN-γ binds to a distinct type II receptor. The presence and number of IFN receptors on the surface of a cell does not generally reflect the sensitivity of the cell to IFN, although it is clear that the effects of the IFN protein is mediated through binding to a cell surface interferon receptor. As such, the identification and characterization of novel interferon receptor proteins is of extreme interest.

We herein describe the identification and characterization of novel interferon receptor polypeptides, designated herein as "PRO1114 interferon receptor" polypeptides. Thus, the PRO1114 polypeptides of the present invention represents a novel cell surface interferon receptor.

47. **PRO828**

Glutathione peroxidases are of interest because they play important roles in protection against risk of coronary disease, atherosclerosis, platelet hyperaggregation and synthesis of proaggregant and proinflammatory compounds. Glutathione peroxidases are involved in the reduction of hydrogen peroxides and lipid peroxides, which in turn regulate the activities of cyclooxygenase and lipooxygenase pathways. This ultimately influences the production of eicosanoids and modulates the balance between a proaggregatory and antiaggregatory state of platelets. These and other activities and functions of glutathione peroxidases are discussed in greater detail by Ursini et al., Biomed. Environ. Sci 10(2-3): 327-332 (1997); Vitoux et al., Ann. Biol. Clin (Paris) 54(5): 181-187 (1996); and Mirault et al., Ann N.Y. Acad. Sci 738: 104-115 (1994).

We herein describe the identification and characterization of novel polypeptides having sequence identity with glutathione peroxidases, designated herein as PRO828 polypeptides.

48. **PRO1009**

Long chain acyl-CoA synthetase converts free fatty acids to acyl-CoA esters. This synthetase has been reported to have interesting characteristics. Specifically, it has been reported that two boys having Alport syndrome, elliptocytosis and mental retardation carried a large deletion where long chain acyl-CoA synthetase 4 would have been located. Thus, the absence of this enzyme is believed to play a role in the development of mental retardation or other signs associated with Alport syndrome in the family. Piccini, et al., Genomics, 47(3):350-358 (1998). Moreover, it has been reported that an inhibitor of acyl coenzyme A synthetase, triacsin

C, inhibits superoxide anion generation and degranulation by human neutrophils. Thus, it is suggested that there is a role for acyl-CoA esters in regulating activation of O_2 generation and degranulation at the G protein or subsequent step(s). Korchak, et al., J. Biol. Chem., 269(48):30281-30287 (1994). Long chain acyl-CoA synthetase is also briefly discussed in a report which describes very long chain acyl-CoA synthetase. Uchiyama, et al., J. Biol. Chem., 271(48):30360 (1994). Thus, long chain acyl-CoA synthetase and particular novel polypeptides having sequence identity therewith are of interest.

We herein describe the identification and characterization of novel polypeptides having sequence identity with long chain acyl-CoA synthetase, designated herein as PRO1009 polypeptides.

49. PRO1007

Glycosylphosphatidylinositol (GPI) anchored proteoglycans are generally localized to the cell surface and are thus known to be involved in the regulation of responses of cells to numerous growth factors, cell adhesion molecules and extracellular matrix components. The metastasis-associated GPI-anchored protein (MAGPIAP) is one of these cell surface proteins which appears to be involved in metastasis. Metastasis is the form of cancer wherein the transformed or malignant cells are traveling and spreading the cancer from one site to another. Therefore, identifying the polypeptides related to metastasis and MAGPIAP is of interest.

We herein describe the identificationand characterization of novel polypeptides having sequence identity with MAGPIAP, designated herein as PRO1007 polypeptides.

50. PRO1056

Mammalian cell membranes perform very important functions relating to the structural integrity and activity of various cells and tissues. Of particular interest in membrane physiology is the study of trans-membrane ion channels which act to directly control a variety of physiological, pharmacological and cellular processes. Numerous ion channels have been identified including calcium (Ca), sodium (Na), chloride (Cl) and potassium (K) channels, each of which have been analyzed in detail to determine their roles in physiological processes in vertebrate and insect cells. These roles include such things as maintaining cellular homeostasis, intracellular signaling, and the like. Given the obvious importance of the ion channels, there is significant interest in identifying and characterizing novel polypeptides having homology to one or more ion channels. We herein describe the identification and characterization of novel polypeptides having homology to a chloride channel protein, designated herein as PRO1056 polypeptides..

51. PRO826

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO826 polypeptides.

52. **PRO819**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO819 polypeptides.

53. **PRO1006**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1006 polypeptides.

54. **PRO1112**

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO1112 polypeptides.

55. **PRO1074**

Many membrane-bound enzymatic proteins play important roles in the chemical reactions involved in metabolism, including the biosynthesis of macromolecules, the controlled release and utilization of chemical energy, development of tissues, and other processes necessary to sustain life. Galactosyltransferases are a family of enzymes that play a variety of important metabolic roles and thus are the subject of interest in research and industry. Numerous references have been published on the identification of galactosyltransferases and the roles they play in cellular development, maintenance, and dysfunction.

We herein describe the identification and characterization of novel polypeptides having homology to galactosyltransferases, designated herein as PRO1074 polypeptides.

56. **PRO1005**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1005 polypeptides.

57. **PRO1073**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel

secreted polypeptides, designated herein as PRO1073 polypeptides.

58. PRO1152

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO1152 polypeptides.

59. PRO1136

PDZ domain-containing proteins assist formation of cell-cell junctions and localization of membrane protein receptors and ion channels (Daniels et al., Nat. Struct. Biol. 5:317-325 (1998) and Ullmer et al., FEBS Lett. 424:63-68 (1998)). PDZ domains interact with the C-terminal residues of a particular target membrane protein. Based on their binding specificities and sequence homologies, PDZ domains fall into two classes, class I and class II. In light of the obvious importance of the PDZ domain-containing proteins, there is significant interest in identifying novel polypeptides that have homology to those proteins. We herein describe the identification and characterization of novel polypeptides having homology to PDZ domain-containing proteins, designated herein as PRO1136 polypeptides.

60. PRO813

Surfactant proteins play extremely important biological roles in the mammalian pulmonary system. One mammalian protein that has been studied and well characterized is pulmonary surfactant-associated protein C. For example, Qanbar et al., Am. J. Physiol. 271:L572-L580 (1996) studied the effect of palmitoylation of pulmonary surfactant-associated protein C on the surface activity of phospholipid mixtures. Specifically, the authors demonstrated that palmitoylation of pulmonary surfactant-associated protein C greatly enhanced lipid respreading and film stability and, therefore, was extremely important for surfactant function. Given the obvious important roles played by surfactant protein in the mammalian organism, there is significant interest in identifying novel polypeptides having homology to one or more surfactant enzymes. We herein describe the identification and characterization of novel polypeptides having homology to pulmonary surfactant-associated protein, designated herein as PRO813 polypeptides.

61. PRO809

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO809 polypeptides.

62. PRO791

Of particular interest are novel proteins which have sequence identity with known proteins. For example, novel proteins having some sequence identity with the major histocompatibility complex (MHC) are of interest. The MHC complex is a region of multiple loci that play major roles in determining whether transplanted tissue will be accepted as self (histocompatible) or rejected as foreign (histoincompatible). Moreover, the MHC plays a central role in the development of both humoral and cell-mediated immune responses. There are class I, II and III MHC antigens, all known in the art. Class I antigens are glycoproteins expressed on the surface of nearly all nucleated cells, where they present peptide antigens of altered self-cells necessary for the activation of Tc cells. The assembly of MHC class I antigens is further described in Kvist and Levy, Semin. Immunol., 5(2):105-116 (1993) and Maffei, et al., Hum. Immunol., 54(2):91-103 (1997).

We herein describe the identification and characterization of novel polypeptides having sequence identity to various MHC-I antigens, designated herein as PRO791 polypeptides.

63. PRO1004

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1004 polypeptides.

64. PRO1111

Protein-protein interactions include receptor and antigen complexes and signaling mechanisms. As more is known about the structural and functional mechanisms underlying protein-protein interactions, protein-protein interactions can be more easily manipulated to regulate the particular result of the protein-protein interaction. Thus, the underlying mechanisms of protein-protein interactions are of interest to the scientific and medical community.

All proteins containing leucine-rich repeats are thought to be involved in protein-protein interactions. Leucine-rich repeats are short sequence motifs present in a number of proteins with diverse functions and cellular locations. The crystal structure of ribonuclease inhibitor protein has revealed that leucine-rich repeats correspond to beta-alpha structural units. These units are arranged so that they form a parallel beta-sheet with one surface exposed to solvent, so that the protein acquires an unusual, nonglubular shape. These two features have been indicated as responsible for the protein-binding functions of proteins containing leucine-rich repeats. See, Kobe and Deisenhofer, Trends Biochem. Sci., 19(10):415-421 (Oct. 1994).

A study has been reported on leucine-rich proteoglycans which serve as tissue organizers, orienting and ordering collagen fibrils during ontogeny and are involved in pathological processes such as wound healing, tissue repair, and tumor stroma formation. Iozzo, R. V., Crit. Rev. Biochem. Mol. Biol., 32(2):141-174 (1997). Others studies implicating leucine rich proteins in wound healing and tissue repair are De La Salle, C., et al., Vouv. Rev. Fr. Hematol. (Germany), 37(4):215-222 (1995), reporting mutations in the leucine rich motif in a complex associated with the bleeding disorder Bernard-Soulier syndrome, Chlemetson, K. J., Thromb.

Haemost. (Germany), 74(1):111-116 (July 1995), reporting that platelets have leucine rich repeats and Ruoslahti, E. I., et al., WO9110727-A by La Jolla Cancer Research Foundation reporting that decorin binding to transforming growth factorβ has involvement in a treatment for cancer, wound healing and scarring. Related by function to this group of proteins is the insulin like growth factor (IGF), in that it is useful in wound-healing and associated therapies concerned with re-growth of tissue, such as connective tissue, skin and bone; in promoting body growth in humans and animals; and in stimulating other growth-related processes. The acid labile subunit of IGF (ALS) is also of interest in that it increases the half-life of IGF and is part of the IGF complex in vivo.

Another protein which has been reported to have leucine-rich repeats is the SLIT protein which has been reported to be useful in treating neuro-degenerative diseases such as Alzheimer's disease, nerve damage such as in Parkinson's disease, and for diagnosis of cancer, see, Artavanistsakonas, S. and Rothberg, J. M., WO9210518-A1 by Yale University. Of particular interest is LIG-1, a membrane glycoprotein that is expressed specifically in glial cells in the mouse brain, and has leucine rich repeats and immunoglobulin-like domains. Suzuki, et al., J. Biol. Chem. (U.S.), 271(37):22522 (1996). Other studies reporting on the biological functions of proteins having leucine rich repeats include: Tayar, N., et al., Mol. Cell Endocrinol., (Ireland), 125(1-2):65-70 (Dec. 1996) (gonadotropin receptor involvement); Miura, Y., et al., Nippon Rinsho (Japan), 54(7):1784-1789 (July 1996) (apoptosis involvement); Harris, P. C., et al., J. Am. Soc. Nephrol., 6(4):1125-1133 (Oct. 1995) (kidney disease involvement).

We herein describe the identification and characterization of novel polypeptides having homology to LIG, designated herein as PRO1111 polypeptides.

65. **PRO1344**

Factor C is a protein that is intimately involved with the coagulation cascade in a variety of organisms. The coagulation cascade has been shown to involve numerous different intermediate proteins, including factor C, all of whose activity is essential to the proper functioning of this cascade. Abnormal coagulation cascade function can result in a variety of serious abnormalities and, as such, the activities of the coagulation cascade proteins is of particular interest. As such, efforts are currently being undertaken to identify novel polypeptides having homology to one or more of the coagulation cascade proteins.

We herein describe the identification and characterization of novel polypeptides having homology to factor C protein, designated herein as PRO1344 polypeptides.

66. **PRO1109**

Carbohydrate chains on glycoproteins are important not only for protein conformation, transport and stability, but also for cell-cell and cell-matrix interactions. β-1,4-galactosyltransferase is an enzyme that is involved in producing carbohydrate chains on proteins, wherein the β-1,4-galactosyltransferase enzyme acts to transfer galactose to the terminal N-acetylglucosamine of complex-type N-glycans in the Golgi apparatus (Asano et al., EMBO J. 16:1850-1857 (1997)). In addition, it has been suggested that β-1,4-galactosyltransferase is invloved directly in cell-cell interactions during fertilization and early embryogenesis through a subpopulation of this enzyme distributed on the cell surface. Specifically, Lu et al., Development 124:4121-4131 (1997) and

Larson et al., Biol. Reprod. 57:442-453 (1997) have demonstrated that β-1,4-galactosyltransferase is expressed on the surface of sperm from a variety of mammalian species, thereby suggesting an important role in fertilization. In light of the above, novel polypeptides having sequence identity to β-1,4-galactosyltransferase are of interest.

We herein describe the identification and characterization of novel polypeptides having homology to β-1,4-galactosyltransferase, designated herein as PRO1109 polypeptides.

67. PRO1383

The nmb gene is a novel gene that encodes a putative transmembrane glycoprotein which is differentially expressed in metastatic human melanoma cell lines and which shows substantial homology to the precursor of pMEL17, a melanocyte-specific protein (Weterman et al., Int. J. Cancer 60:73-81 (1995)). Given the interest in identifying tumor-specific cell-surface polypeptide markers, there is substantial interest in novel polypeptides having homology to nmb. We herein describe the identification and characterization of novel polypeptides having homology to the nmb protein, designated herein as PRO1383 polypeptides.

68. PRO1003

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1003 polypeptides.

69. PRO1108

Lysophosphatidic acid acyltransferase (LPAAT) is an enzyme that in lipid metabolism converts lysophosphatidic acid (LPA) into phosphatidic acid (PA). LPA is a phospholipid that acts as an intermediate in membrane phospholipid metabolism. Various LPAAT enzymes have been identified in a variety of species (see, e.g., Aguado et al., J. Biol. Chem. 273:4096-4105 (1998), Stamps et al., Biochem. J. 326:455-461 (1997), Eberhart et al., J. Biol. Chem. 272:20299-20305 (1997) and West et al., DNA Cell Biol. 16:691-701 (1997)). Given the obvious importance of LPAAT in a variety of different applications including cell membrane maintenance, there is substantial interest in identifying and characterizing novel polypeptides having homology to LPAAT. We herein describe the identification and characterization of novel polypeptides having homology to LPAAT protein, designated herein as PRO1108 polypeptides.

70. PRO1137

A particular class of secreted polypeptides that are of interest in research and industry are ribosyltransferases. Braren et al. described the use of EST databases for the identification and cloning of novel ribosyltransferase gene family members (Adv. Exp. Med. Biol. 419:163-168 (1997)). Ribosyltransferases have been identified playing roles in a variety of metabolic functions including posttranslational modification of proteins (Saxty et al., J. Leukoc. Biol., 63(1):15-21 (1998)), and mediation of the assembly of filamentous actin

and chemotaxis in polymorphonuclear neutrophil leukocytes (Kefalas et al. Adv. Exp. Med. Biol. 419:241-244 (1997)).

Described herein is the identification and characterization of novel polypeptides having homology to ribosyltransferase, designated herein as PRO1137 polypeptides.

71. **PRO1138**

Efforts are being undertaken by both industry and academia to identify new, native receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins. Of particular interest is the identification of membrane-bound proteins found in cells of the hematopoietic system, as they often play important roles in fighting infection, repair of injured tissues, and other activities of cells of the hematopoietic system. For instance, CD84 leukocyte antigen has recently been identified as a new member of the Ig superfamily (de la Fuente *et al.*, Blood, 90(6):2398-2405 (1997)).

Described herein is the identification and characterization of a novel polypeptide having homology to CD84 leukocyte antigen, designated herein as PRO1138 polypeptides.

72. **PRO1054**

The proteins of the major urinary protein complex (MUP), proteins which are members of the lipocalin family, function to bind to volatile pheromones and interact with the vomeronasal neuroepithelium of the olfactory system. As such, proteins in the MUP family are intimately involved in the process of attraction between mammals of different sexes. Many different MUP family members have been identified and characterized and shown to possess varying degrees of amino acid sequence homology (see, e.g., Mucignat et al., Chem. Senses 23:67-70 (1998), Ferrari et al., FEBS Lett. 401:73-77 (1997) and Bishop et al., EMBO J. 1:615-620 (1982)). Given the physiological and biological importance of the MUP family of proteins, there is significant interest in identifying and characterizing novel members of this family. We herein describe the identification and characterization of novel polypeptides having homology to MUP family of proteins, designated herein as PRO1054 polypeptides.

73. **PRO994**

The L6 cell surface antigen, which is highly expressed on lung, breast, colon, and ovarian carcinomas, has attracted attention as a potential therapeutic target for murine monoclonal antibodies and their humanized counterparts (Marken et al., Proc. Natl. Acad. Sci. USA 89:3503-3507 (1992)). The cDNA encoding this tumor-associated cell surface antigen has been expressed in COS cells and shown to encode a 202 amino acid polypeptide having three transmembrane domains. The L6 antigen has been shown to be related to a number of cell surface proteins that have been implicated in the regulation of cell growth, including for example CD63 and CO-029, proteins which are also highly expressed on tumor cells. As such, there is significant interest in identifying novel polypeptides having homology to the L6 tumor cell antigen as potential targets for cancer therapy. We herein describe the identification and characterization of novel polypeptides having homology to

the L6 cell surface tumor cell-associated antigen, designated herein as PRO994 polypeptides.

74. **PRO812**

Steroid binding proteins play important roles in numerous physiological processes associated with steroid function. Specifically, one steroid binding protein-associated polypeptide that has been well characterized is component 1 of the prostatic binding protein. Component 1 of the prostatic binding protein has been shown to be specific for subunit F of the prostatic binding protein, the major secretory glycoprotein of the rat ventral prostate (Peeters et al., Eur. J. Biochem. 123:55-62 (1982) and Liao et al., J. Biol. Chem. 257:122-125 (1982)). The amino acid sequence of component 1 of the prostatic binding protein has been determined, wherein the sequence is highly rich in glutamic acid residues and is overall highly acidic. This protein plays an important role in the response of the prostate gland to steroid hormones. We herein describe the identification and characterization of novel polypeptides having homology to prostatic steroid-binding protein c1, designated herein as PRO812 polypeptides.

75. **PRO1069**

Of particular interest is the identification of new membrane-bound proteins involved in ion conductance such as channel inhibitory factor (CHIF) and MAT-8, which have recently been reported (see Wald et al., Am. J. Physiol, 272(5 pt 2): F617-F623 (1997); Capurro et al., Am. J. Physiol, 271(3 pt 1): C753-C762 (1996); Wald et al., Am. J. Physiol, 271(2 pt 2): F322-F329 (1996); and Morrison et al., J. Biol. Chem 270(5):2176-2182 (1995)).

Described herein is the identification and characterization of novel polypeptides having homology to CHIF and MAT-8 polypeptides, designated herein as PRO1069 polypeptides.

76. **PRO1129**

Cytochromes P-450 are a superfamily of hemoproteins which represent the main pathway for drug and chemical oxidation (Horsmans, Acta Gastroenterol. Belg. 60:2-10 (1997)). This superfamily is divided into families, subfamilies and/or single enzymes. Recent reports have provided a great deal of information concerning the cytochrome P-450 isozymes and increased awareness of life threatening interactions with such commonly prescribed drugs as cisapride and some antihistamines (Michalets, Pharmacotherapy 18:84-112 (1998) and Singer et al., J. Am. Acad. Dermatol. 37:765-771 (1997)). Given this information, there is significant interest in identifying novel members of the cytochrome P-450 family of proteins. We herein describe the identification and characterization of novel polypeptides having homology to cytochrome P-450 proteins, designated herein as PRO1129 polypeptides.

77. **PRO1068**

Urotensins are neurosecretory proteins that are of interest because of their potential roles in a variety of physiological processes including smooth muscle contraction (Yano et al. Gen. Comp. Endocrinol. 96(3): 412-413 (1994)), regulation of arterial blood pressure and heart rate (Le Mevel et al. Am. J. Physiol. 271(5 Pt 2):

R1335-R1343 (1996)), and corticosteroid secretion (Feuilloley et al. J. Steroid Biochem Mol. Biol. 48(2-3): 287-292 (1994)).

We herein describe the identification and characterization of novel polypeptides having homology to urotensin, designated herein as PRO1068 polypeptides.

78. **PRO1066**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1066 polypeptides.

79. **PRO1184**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1184 polypeptides.

80. **PRO1360**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1360 polypeptides.

81. **PRO1029**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1029 polypeptides.

82. **PRO1139**

Obesity is the most common nutritional disorder which, according to recent epidemiologic studies, affects about one third of all Americans 20 years of age or older. Kuczmarski et al., J. Am. Med. Assoc. 272, 205-11 (1994). Obesity is responsible for a variety of serious health problems, including cardiovascular disorders, type II diabetes, insulin-resistance, hypertension, hypertriglyceridemia, dyslipoproteinemia, and some forms of cancer. Pi-Sunyer, F.X., Anns. Int. Med. 119, 655-60 (1993); Colfitz, G.A., Am. J. Clin. Nutr. 55, 503S-507S (1992). A single-gene mutation (the obesity or "*ob*" mutation) has been shown to result in obesity and type II diabetes in mice. Friedman, Genomics 11, 1054-1062 (1991). Zhang et al., Nature 372, 425-431 (1994) have recently reported the cloning and sequencing of the mouse *ob* gene and its human homologue, and

suggested that the ob gene product may function as part of a signaling pathway from adipose tissue that acts to regulate the size of the body fat depot. Parabiosis experiments performed more than 20 years ago predicted that the genetically obese mouse containing two mutant copies of the *ob* gene (*ob/ob* mouse) does not produce a satiety factor which regulates its food intake, while the diabetic (*db/db*) mouse produces but does not respond to a satiety factor. Coleman and Hummal, Am. J. Physiol. 217, 1298-1304 (1969); Coleman, Diabetol. 9, 294-98 (1973). OB proteins are disclosed, for example, in U.S. patent Nos. 5,532,336; 5,552,522; 5,552,523; 5,552,514; 5,554,727. Recent reports by three independent research teams have demonstrated that daily injections of recombinant OB protein inhibit food intake and reduce body weight and fat in grossly obese *ob/ob* mice but not in *db/db* mice (Pelleymounter et al., Science 269, 540-43 [1995]; Halaas et al., Science 269, 543-46 [1995]; Campfield et al., Science 269, 546-49 [1995]), suggesting that the *ob* protein is such a satiety factor as proposed in early cross-circulation studies.

A receptor of the OB protein (OB-R) is disclosed in Tartaglia et al., Cell 83, 1263-71 (1995). The OB-R is a single membrane-spanning receptor homologous to members of the class I cytokine receptor family (Tartaglia et al., supra; Bazan, Proc. Natl. Acad. Sci. USA 87, 6934-6938 [1990]). Two 5'-untranslated regions and several 3'-alternative splice variants encoding OB-R with cytoplasmic domains of different lengths have been described in mouse, rat and human (Chen et al., Cell 84, 491-495 [1996]; Chua et al., Science 271, 994-996 [1996]; Tartaglia et al., supra; Wang et al., FEBS Lett. 392:87-90 [1996]; Phillips et al., Nature Genet. 13, 18-19 [1996]; Cioffi et al., Nature Med., 2 585-589 [1996]). A human hematopoetin receptor, which might be a receptor of the OB protein, is described in PCT application Publication No. WO 96/08510, published 21 March 1996.

Bailleul et al., Nucl. Acids Res. 25, 2752-2758 (1997) identified a human mRNA splice variant of the OB-R gene that potentially encodes a novel protein, designated as leptin receptor gene-related protein (OB-RGRP). This protein displays no sequence similarity to the leptin receptor itself. The authors found that the OB-RGRP gene shares its promoter and two exons with the OB-R gene, and suggested that there is a requirement for a coordinate expression of OB-R and OB-RGRP to elicit the full physiological response to leptin *in vivo*.

83. **PRO1309**

Protein-protein interactions include receptor and antigen complexes and signaling mechanisms. As more is known about the structural and functional mechanisms underlying protein-protein interactions, protein-protein interactions can be more easily manipulated to regulate the particular result of the protein-protein interaction. Thus, the underlying mechanisms of protein-protein interactions are of interest to the scientific and medical community.

All proteins containing leucine-rich repeats are thought to be involved in protein-protein interactions. Leucine-rich repeats are short sequence motifs present in a number of proteins with diverse functions and cellular locations. The crystal structure of ribonuclease inhibitor protein has revealed that leucine-rich repeats correspond to beta-alpha structural units. These units are arranged so that they form a parallel beta-sheet with one surface exposed to solvent, so that the protein acquires an unusual, nonglubular shape. These two features have been indicated as responsible for the protein-binding functions of proteins containing leucine-rich repeats.

See, Kobe and Deisenhofer, Trends Biochem. Sci., 19(10):415-421 (Oct. 1994); Kobe and Deisenhofer, Curr. Opin. Struct. Biol., 5(3):409-416 (1995).

A study has been reported on leucine-rich proteoglycans which serve as tissue organizers, orienting and ordering collagen fibrils during ontogeny and are involved in pathological processes such as wound healing, tissue repair, and tumor stroma formation. Iozzo, R. V., Crit. Rev. Biochem. Mol. Biol., 32(2):141-174 (1997). Others studies implicating leucine rich proteins in wound healing and tissue repair are De La Salle, C., et al., Vouv. Rev. Fr. Hematol. (Germany), 37(4):215-222 (1995), reporting mutations in the leucine rich motif in a complex associated with the bleeding disorder Bernard-Soulier syndrome, Chlemetson, K. J., Thromb. Haemost. (Germany), 74(1):111-116 (July 1995), reporting that platelets have leucine rich repeats and Ruoslahti, E. I., et al., WO9110727-A by La Jolla Cancer Research Foundation reporting that decorin binding to transforming growth factorβ has involvement in a treatment for cancer, wound healing and scarring. Related by function to this group of proteins is the insulin like growth factor (IGF), in that it is useful in wound-healing and associated therapies concerned with re-growth of tissue, such as connective tissue, skin and bone; in promoting body growth in humans and animals; and in stimulating other growth-related processes. The acid labile subunit of IGF (ALS) is also of interest in that it increases the half-life of IGF and is part of the IGF complex in vivo.

Another protein which has been reported to have leucine-rich repeats is the SLIT protein which has been reported to be useful in treating neuro-degenerative diseases such as Alzheimer's disease, nerve damage such as in Parkinson's disease, and for diagnosis of cancer, see, Artavanistsakonas, S. and Rothberg, J. M., WO9210518-A1 by Yale University. Of particular interest is LIG-1, a membrane glycoprotein that is expressed specifically in glial cells in the mouse brain, and has leucine rich repeats and immunoglobulin-like domains. Suzuki, et al., J. Biol. Chem. (U.S.), 271(37):22522 (1996). Other studies reporting on the biological functions of proteins having leucine rich repeats include: Tayar, N., et al., Mol. Cell Endocrinol., (Ireland), 125(1-2):65-70 (Dec. 1996) (gonadotropin receptor involvement); Miura, Y., et al., Nippon Rinsho (Japan), 54(7):1784-1789 (July 1996) (apoptosis involvement); Harris, P. C., et al., J. Am. Soc. Nephrol., 6(4):1125-1133 (Oct. 1995) (kidney disease involvement).

Efforts are therefore being undertaken by both industry and academia to identify new proteins having leucine rich repeats to better understand protein-protein interactions. Of particular interest are those proteins having leucine rich repeats and homology to known proteins having leucine rich repeats such as platelet glycoprotein V, SLIT and ALS. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins having leucine rich repeats.

84. PRO1028

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1028 polypeptides.

85. PRO1027

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1027 polypeptides.

86. PRO1107

Of particular interest are novel proteins having some sequence identity to known proteins. Known proteins include PC-1, an ecto-enzyme possessing alkaline phosphodiesterase I and nucleotide pyrophosphatase activities, further described in Belli et al., Eur. J. Biochem., 228(3):669-676 (1995). Phosphodiesterases are also described in Fuss et al., J. Neurosci., 17(23):9095-9103 (1997) and Scott et al., Hepatology, 25(4):995-1002 (1997). Phosphodiesterase I, is described as a novel adhesin molecule and/or cytokine (related to autotaxin) involved in oligodendrocyte function. Fuss, supra.

We herein describe the identification and characterization of novel polypeptides having homology nto PC-1, designated herein as PRO1107 polypeptides.

87. PRO1140

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO1140 polypeptides.

88. PRO1106

As the mitochondria is primarily responsible for generating energy, proteins associated with the mitochondria are of interest. Recently, a cDNA from a novel Ca^{++}-dependent member of the mitochondrial solute carrier superfamily was isolated from a rabbit small intestinal cDNA library as described in Weber, et al., PNAS USA, 94(16):8509-8514 (1997). It was reported that this transporter has four elongation factor-hand motifs in the N-terminal and is localized in the peroxisome, although a fraction can be found in the mitochondria. Thus, this transporter, and proteins which have sequence identity to this and other members of the mitochondrial solute carrier superfamily are of particular interest.

We herein describe the identification and characterization of novel polypeptides having homology to a peroxisomal calcium dependent solute carrier protein, designated herein as PRO1106 polypeptides.

89. PRO1291

Butyrophilin is a milk glycoprotein that constitutes more than 40% of the total protein associated with the fat globule membrane in mammalian milk. Expression of butyrophilin mRNA has been shown to correlate with the onset of milk fat production toward the end pregnancy and is maintained throughout lactation. Butyrophilin has been identified in bovine, murine and human (see Taylor et al., Biochim. Biophys. Acta

1306:1-4 (1996), Ishii et al., Biochim. Biophys. Acta 1245:285-292 (1995), Mather et al., J. Dairy Sci. 76:3832-3850 (1993) and Banghart et al., J. Biol. Chem. 273:4171-4179 (1998)) and is a type I transmembrane protein that is incorporated into the fat globulin membrane. It has been suggested that butyrophilin may play a role as the principle scaffold for the assembly of a complex with xanthine dehydrogenase/oxidase and other proteins that function in the budding and release of milk-fat globules from the apical surface during lactation (Banghart et al., supra).

Given that butyrophilin plays an obviously important role in mammalian milk production, there is substantial interest in identifying novel butyrophilin homologs. We herein describe the identification and characterization of novel polypeptides having homology to butyrophilin, designated herein as PRO1291 polypeptides.

90. PRO1105

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO1105 polypeptides.

91. PRO511

Proteins of interest include those having sequence identity with RoBo-1, a novel member of the urokinase plasminogen activator receptor/CD59/Ly-6/snake toxin family selectively expressed in bone and growth plate cartilage as described in Noel et al., J. Biol. Chem. 273(7):3878-3883 (1998). RoBo-1 is believed to play a novel role in the growth or remodeling of bone. Proteins also of interest include those having sequence identity with phospholipase inhibitors.

We herein describe the identification and characterization of novel polypeptides having homology to urokinase plasminogen activator receptors and phospholipase inhibitors, designated herein as PRO511 polypeptides.

92. PRO1104

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1104 polypeptides.

93. PRO1100

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO1100 polypeptides.

94. PRO836

Of interest are luminal proteins, or proteins specific to the endoplasmic reticulum (ER). Of particular interest are proteins having sequence identity with known proteins. Known proteins include proteins such as SLS1. In *Saccharomyces cerevisiae*, SLS1 has been reported to be a mitochondrial integral membrane protein involved in mitochondrial metabolism. Rouillard, et al., Mol. Gen. Genet., 252(6):700-708 (1996). In yeast *Yarrowia lipolytica*, it has been reported that the SLS1 gene product (SLS1p) behaves as a lumenal protein of the ER. It is believed that SPS1p acts in the preprotein translocation process, interacting directly with translocating polypeptides to facilitate their transfer and/or help their folding in the ER. Bosirame, et al., J. Biol. Chem., 271(20):11668-11675 (1996).

We herein describe the identification and characterization of novel polypeptides having homology to SLS1, designated herein as PRO836 polypeptides.

95. PRO1141

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO1141 polypeptides.

96. PRO1132

Proteases are enzymatic proteins which are involved in a large number of very important biological processes in mammalian and non-mammalian organisms. Numerous different protease enzymes from a variety of different mammalian and non-mammalian organisms have been both identified and characterized, including the serine proteases which exhibit specific activity toward various serine-containing proteins. The mammalian protease enzymes play important roles in biological processes such as, for example, protein digestion, activation, inactivation, or modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes.

Neuropsin is a novel serine protease whose mRNA is expressed in the central nervous system. Mouse neuropsin has been cloned, and studies have shown that it is involved in the hippocampal plasticity. Neuropsin has also been indicated as associated with extracellular matrix modifications and cell migrations. See, generally, Chen, et al., Neurosci., 7(2):5088-5097 (1995) and Chen, et al., J. Histochem. Cytochem., 46:313-320 (1998).

Another serine protease of interest is the enamel matrix serine proteinase. The maturation of dental enamel succeeds the degradation of organic matrix. Inhibition studies have shown that this degradation is accomplished by a serine-type proteinase. Proteases associated with enamel maturation are described in, i.e., Simmer, et al., J. Dent. Res., 77(2):377-386 (1998), Overall and Limeback, Biochem J., 256(3):965-972 (1988), and Moradian-Oldak, Connect. Tissue Res., 35(1-4):231-238 (1996).

We herein describe the identification and characterization of novel polypeptides having homology to serine proteases, designated herein as PRO1132 polypeptides.

97. PRO1346

The abbreviations "TIE" or "tie" are acronyms, which stand for "tyrosine kinase containing Ig and EGF homology domains" and were coined to designate a new family of receptor tyrosine kinases which are almost exclusively expressed in vascular endothelial cells and early hemopoietic cells, and are characterized by the presence of an EGF-like domain, and extracellular folding units stabilized by intra-chain disulfide bonds, generally referred to as "immunoglobulin (IG)-like" folds. A tyrosine kinase homologous cDNA fragment from human leukemia cells (tie) was described by Partanen et al., Proc. Natl. Acad. Sci. USA 87, 8913-8917 (1990). The mRNA of this human "TIE" receptor has been detected in all human fetal and mouse embryonic tissues, and has been reported to be localized in the cardiac and vascular endothelial cells. Korhonen et al., Blood 80, 2548-2555 (1992); PCT Application Publication No. WO 93/14124 (published 22 July 1993). The rat homolog of human TIE, referred to as "TIE-1", was identified by Maisonpierre et al., Oncogene 8, 1631-1637 (1993)). Another TIE receptor, designated "TIE-2" was originally identified in rats (Dumont et al., Oncogene 8, 1293-1301 (1993)), while the human homolog of TIE-2, referred to as "ork" was described in U.S. Patent No. 5,447,860 (Ziegler). The murine homolog of TIE-2 was originally termed "tek." The cloning of a mouse TIE-2 receptor from a brain capillary cDNA library is disclosed in PCT Application Publication No. WO 95/13387 (published 18 May 1995). TIE-2 is a receptor tyrosine kinase that is expressed almost exclusively by vascular endothelium. Tie-2 knockout mice die by defects in the formation of microvassels. Accordingly, the TIE receptors are believed to be actively involved in angiogenesis, and may play a role in hemopoiesis as well. Indeed, recent results (Lin *et al.*, J. Clin. Invest. 100(8), 2072-2078 [1997]) demonstrating the ability of a soluble TIE-2 receptor to inhibit tumor angiogenesis have been interpreted to indicate that TIE-2 plays a role in pathologic vascular growth. In another study, TIE-2 expression was examined in adult tissues undergoing angiogenesis and in quiescent tissues. TIE2 expression was localized by immunohistochemistry to the endothelium of neovessels in rat tissues undergoing angiogenesis during hormonally stimulated follicular maturation and uterine development and in healing wounds. TIE-2 was also reported to be expressed in the entire spectrum of the quiescent vasculature (arteries, veins, and capillaries) in a wide range of adult tissues. Wong *et al.*, Circ. Res. 81(4), 567-574 (1997). It has been suggested that TIE-2 has a dual function in adult angiogenesis and vascular maintenance.

The expression cloning of human TIE-2 ligands has been described in PCT Application Publication No. WO 96/11269 (published 18 April 1996) and in U.S. Patent No. 5,521,073 (published 28 May 1996). A vector designated as λgt10 encoding a TIE-2 ligand NL7d "htie-2 ligand 1" or "hTL1" has been deposited under ATCC Accession No. 75928. A plasmid encoding another TIE-2 ligand designated "htie-2 2" or "hTL2" is available under ATCC Accession No. 75928. This second ligand has been described as an antagonist of the TAI-2 receptor. The identification of secreted human and mouse ligands for the TIE-2 receptor has been reported by Davis et al., Cell 87, 1161-1169 (1996). The human ligand designated "Angiopoietin-1", to reflect its role in angiogenesis and potential action during hemopoiesis, is the same ligand as the ligand variously designated as "htie-2 1" or "hTL-1" in WO 96/11269. Angiopoietin-1 has been described to play an angiogenic role later and distinct from that of VEGF (Suri et al., Cell 87, 1171-1180 (1996)). Since TIE-2 is apparently upregulated during the pathologic angiogenesis requisite for tumor growth (Kaipainen et al., Cancer Res. 54, 6571-6577

(1994)) angiopoietin-1 has been suggested to be additionally useful for specifically targeting tumor vasculature (Davis et al., supra).

We herein describe the identification and characterization of novel TIE ligand polypeptides, designated herein as PRO1346 polypeptides.

98. PRO1131

The low density lipoprotein (LDL) receptor is a membrane-bound protein that plays a key role in cholesterol homeostasis, mediating cellular uptake of lipoprotein particles by high affinity binding to its ligands, apolipoprotein (apo) B-100 and apoE. The ligand-binding domain of the LDL receptor contains 7 cysteine-rich repeats of approximately 40 amino acids, wherein each repeat contains 6 cysteines, which form 3 intra-repeat disulfide bonds. These unique structural features provide the LDL receptor with its ability to specifically interact with apo B-100 and apoE, thereby allowing for transport of these lipoprotein particles across cellular membranes and metabolism of their components. Soluble fragments containing the extracellular domain of the LDL receptor have been shown to retain the ability to interact with its specific lipoprotein ligands (Simmons et al., J. Biol. Chem. 272:25531-25536 (1997)). LDL receptors are further described in Javitt, FASEB J., 9(13):1378-1381 (1995), van Berkel, et al., Atherosclerosis, 118 Suppl:S43-S50 (1995) and Herz and Willnow, Ann. NY Acad. Sci., 737:14-19 (1994). Thus, proteins having sequence identity with LDL receptors are of interest.

We herein describe the identification and characterization of novel polypeptides having homology to LDL receptors, designated herein as PRO1131 polypeptides.

99. PRO1281

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1281 polypeptides.

100. PRO1064

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO1064 polypeptides.

101. PRO1379

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1379 polypeptides.

102. PRO844

Proteases are enzymatic proteins which are involved in a large number of very important biological processes in mammalian and non-mammalian organisms. Numerous different protease enzymes from a variety of different mammalian and non-mammalian organisms have been both identified and characterized. The mammalian protease enzymes play important roles in many different biological processes including, for example, protein digestion, activation, inactivation, or modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes. Thus, proteases are of interest. Also of interest are protease inhibitors.

Of particular interest are serine proteases. In one study it was reported that when the serine protease inhibitor antileukoproteinase (aLP) is injected, it accumulates in articular and extraarticular cartilage of normal rats. This physiological pathway of cartilage accumulation, lost in proteoglycan depleted arthritic cartilage is believed to serve to maintain the local balance between proteinase function and inhibition. Burkhardt, et al., J. Rheumatol, 24(6):1145-1154 (1997). Moreover, aLP and other protease inhibitors have been reported to play a role in the in vitro growth of hematopoietc cells by the neutralization of proteinases produced by bone marrow accessory cells. Gosklink, et al., J. Exp. Med., 184(4):1305-1312 (1996). Also of interest are mutants of aLP. Oxidation resistant mutants of aLPe have been reported to have significant therapeutic effects on animal models having emphysema. Steffens, et al., Agents Actions Suppl., 42:111-121 (1993). Thus, serine protease inhibitors are of interest.

We herein describe the identification and characterization of novel polypeptides having homology to serine protease inhibitors, designated herein as PRO844 polypeptides.

103. PRO848

Membrane-bound proteins of interest include channels such as ion channels. Furthermore, membrane-bound proteins of interest include enzymes bound to intracellular vacuoles or organelles, such as transferases. For example, a peptide of interest is the GalNAc alpha 2, 6-sailytransferase as described in Kurosawa, et al., J. Biol. Chem., 269(2):1402-1409 (1994). This peptide was constructed to be secreted, and retained its catalytic activity. The expressed enzyme exhibited activity toward asialomucin and asialofetuin, but not other glycoproteins tested. As sialylation is an important function, sialyltransferases such as this one, and peptides related by sequence identity, are of interest.

We herein describe the identification and characterization of novel polypeptides having homology to sialyltransferases, designated herein as PRO848 polypeptides.

104. PRO1097

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1097 polypeptides.

105. PRO1153

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO1153 polypeptides.

106. PRO1154

Aminopeptidase N causes enzymatic degradation of perorally administered peptide drugs. Thus, aminopeptidase N has been used in studies to develop and identify inhibitors so as to increase the efficacy of peptide drugs by inhibiting their degradation. Aminopeptidases are also generally of interest to use to degrade peptides. Aminopeptidases, particularly novel aminopeptidases are therefore of interest. Aminopeptidase N and inhibitors thereof are further described in Bernkop-Schnurch and Marschutz, Pharm. Res., 14(2):181-185 ((1997); Lerche, et al., Mamm. Genome, 7(9):712-713 (1996); Papapetropoulos, et al., Immunopharmacology, 32(1-3):153-156 (1996); Miyachi, et al., J. Med. Chem., 41(3):263-265 (1998); and Olsen, et al., Adv. Exp. Med. Biol., 421:47-57 (1997).

We herein describe the identification and characterization of novel polypeptides having homology to aminopeptidase N, designated herein as PRO1154 polypeptides.

107. PRO1181

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1181 polypeptides.

108. PRO1182

Conglutinin is a bovine serum protein that was originally described as a vertebrate lectin protein and which belongs to the family of C-type lectins that have four characteristic domains, (1) an N-terminal cysteine-rich domain, (2) a collagen-like domain, (3) a neck domain and (4) a carbohydrate recognition domain (CRD). Recent reports have demonstrated that bovine conglutinin can inhibit hemagglutination by influenza A viruses as a result of their lectin properties (Eda et al., Biochem. J. 316:43-48 (1996)). It has also been suggested that lectins such as conglutinin can function as immunoglobulin-independent defense molecules due to complement-mediated mechanisms. Thus, conglutinin has been shown to be useful for purifying immune complexes *in vitro* and for removing circulating immune complexes from patients plasma *in vivo* (Lim et al., Biochem. Biophys. Res. Commun. 218:260-266 (1996)). We herein describe the identification and characterization of novel polypeptides having homology to conglutinin protein, designated herein as PRO1182 polypeptides.

109. PRO1155

Substance P and the related proteins, neurokinin A and neurokinin B have been reported as compounds which elicit contraction of the ileum both directly through action on a muscle cell receptor and indirectly through stimulation of a neuronal receptor. This action leads to the release of acetylcholine which causes muscle contraction via muscarinic receptors. It has also been reported that neurokinin B was found to be the most potent agonist for the neuronal Substance P receptor and that neurokinin B can be inhibited by enkephalinamide. Laufer, et al., PNAS USA, 82(21):74444-7448 (1985). Moreover, neurokinin B has been reported to provide neuroprotection and cognitive enhancement, and therefore believed to be useful for the treatment of neurodegenerative disorders, including alzheimers disease. Wenk, et al., Behav. Brain Res., 83(1-2):129-133 (1997). Tachykinins are also described in Chawla, et al., J. Comp. Neurol., 384(3):429-442 (1997). Thus, tachykinins, particularly those related to neurokinin B are of interest.

We herein describe the identification and characterization of novel polypeptides having homology to neurokinin B protein, designated herein as PRO1155 polypeptides.

110. PRO1156

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1181 polypeptides.

111. PRO1098

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1098 polypeptides.

112. PRO1127

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1127 polypeptides.

113. PRO1126

The extracellular mucous matrix of olfactory neuroepithelium is a highly organized structure in intimate contact with chemosensory cilia that house the olfactory transduction machinery. The major protein component of this extracellular matrix is olfactomedin, a glycoprotein that is expressed in olfactory neuroepithelium and which form intermolecular disulfide bonds so as to produce a polymer (Yokoe et al., Proc. Natl. Acad. Sci. USA 90:4655-4659 (1993), Bal et al., Biochemistry 32:1047-1053 (1993) and Snyder et al., Biochemistry 30:9143-

9153 (1991)). It has been suggested that olfactomedin may influence the maintenance, growth or differentiation of chemosensory cilia on the apical dendrites of olfactory neurons. Given this important role, there is significant interest in identifying and characterizing novel polypeptides having homology to olfactomedin. We herein describe the identification and characterization of novel polypeptides having homology to olfactomedin protein, designated herein as PRO1126 polypeptides.

114. PRO1125

Of particular interest are proteins which have multiple Trp-Asp (WD) repeats. WD proteins are made up of highly conserved repeating units usually ending with WD. They are found in eukaryotes but not in prokaryotes. They regulate cellular functions, such as cell division, cell-fate determination, gene transcription, gene transcription, transmembrane signaling, mRNA modification and vesicle fusion. WD are further described in Neer, et al., Nature, 371(6495):297-300 (1994); Jiang and Struhl, Nature, 391(6666):493-496(1998); and DeSilva, et al., Genetics, 148(2):657-667 (1998). Thus, new members of this superfamily are all of interest.

115. PRO1186

Protein A from Dendroaspis polylepis polylepis (black mamba) venom comprises 81 amino acids, including ten half-cystine residues. Venoms are of interest on the one hand as weapons in war, and on the other hand, to use in assays to determine agents which reverse or inhibit the effects of the venom or a similar poison. Black mamba venom is further described in Int. J. Biochem., 17(6):695-699 (1985) and Joubert and Strydom, Hoppe Seylers Z Physiol. Chem., 361(12):1787-1794 (1980).

We herein describe the identification and characterization of novel polypeptides having homology to snake venom protein A, designated herein as PRO1186 polypeptides.

116. PRO1198

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1198 polypeptides.

117. PRO1158

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO1158 polypeptides.

118. PRO1159

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the

coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1159 polypeptides.

119. PRO1124

Ion channels are considered to be the gateway to the final frontier, the brain. Ion channels and the receptors which control these channels are responsible for the passage of ions, or nerve impulses to be communicated from cell to cell, thus, ion channels are responsible for communication. In addition to their critical role in the brain, ion channels play a critical role in the heart as well as blood pressure. Ion channels have also been linked to other important bodily functions and conditions, as well as disorders, such as cystic fibrosis. For all of these reasons, ion channels, such as sodium, potassium and chloride channels, as well as all of their related proteins and receptors are of interest. For example, it has been reported that cystic fibrosis results from a defect in the chloride channel protein, cystic fibrosis transmembrane conductance regulator. McGill, et al., Dig. Dis. Sci., 41(3):540-542 (1996). Chloride channels are further described in at least Finn, et al., PNAS USA, 90(12):5691-569 (1993) and Finn, et al., Mol. Cell Biochem., 114(1-2):21-26 (1992).

Also of interest are molecules related to adhesion molecules, as adhesion molecules are known to be involved in cell-cell signaling and interactions. More generally, all novel membrane bound-proteins are of interest. Membrane-bound proteins and receptors can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiationfactors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, channels, transporters, and cellular adhesin molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins include those which are bound to the outer membrane and intracellular membranes and organelles. Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are being undertaken by both industry and academia to identify new, native receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins. Herein is presented a polypeptide and nucleic acid encoding therefor which has sequence identity with a chloride channel protein chloride channel protein and lung-endothelial cell

adhesion molecule-1 (ECAM-1).

120. **PRO1287**

Fringe is a protein which specifically blocks serrate-mediated activation of notch in the dorsal compartment of the Drosophila wing imaginal disc. Fleming et al., Development, 124(15):2973-81 (1997). Therefore, fringe protein is of interest for both its role in development as well as its ability to regulate serrate, particularly serrate's signaling abilities. Also of interest are novel polypeptides which may have a role in development and/or the regulation of serrate-like molecules. Of particular interest are novel polypeptides having homology to fringe.

We herein describe the identification and characterization of novel polypeptides having homology to fringe protein, designated herein as PRO1287 polypeptides.

121. **PRO1312**

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO1312 polypeptides.

122. **PRO1192**

Membrane-bound proteins of myelin are of interest because of their possible implications in various nervous system disorders associated with improper myelination. Myelin is a cellular sheath, formed by glial cells, that surrounds axons and axonal processes that enhances various electrochemical properties and provides trophic support to the neuron. Myelin is formed by Schwann cells in the peripheral nervous system (PNS) and by oligodendrocytes in the central nervous system (CNS). Improper myelination of central and peripheral neurons occurs in a number of pathologies and leads to improper signal conduction within the nervous systems. Among the various demyelinating diseases Multiple Sclerosis is the most notable.

The predominant integral membrane protein of the CNS myelin of amphibians, reptiles, birds and mammals are proteolipid protein (PLP) and P0, the main glycoprotein in PNS myelin. (Schlieess and Stoffel, Biol. Chem. Hoppe Seyler (1991) 372(9):865-874). In view of the importance of membrane-bound proteins of the myelin, efforts are being undertaken by both industry and academia to identify and characterize various myelin proteins (see Stratmann and Jeserich, J. Neurochem (1995) 64(6):2427-2436).

123. **PRO1160**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1160 polypeptides.

124. **PRO1187**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1187 polypeptides.

125. **PRO1185**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1185 polypeptides.

126. **PRO345**

Human tetranectin is a 202 amino acid protein encoded by a gene spanning approximately 12 kbp of DNA (Berglund et al., FEBS Lett. 309:15-19 (1992)). Tetranectin has been shown to be expressed in a variety of tissues and functions primarily as a plasminogen binding protein. Tetranectin has been classified in a distinct group of the C-type lectin superfamily but has structural and possibly functional similarity to the collectin proteins (Nielsen et al., FEBS Lett. 412(2):388-396 (1997)). Recent studies have reported that variability in serum tetranectin levels may be predictive of the presence of various types of cancers including, for example, ovarian and colorectal cancers (Hogdall et al., Acta Oncol. 35:63-69 (1996), Hogdall et al., Eur. J. Cancer 31A(6):888-894 (1995) and Tuxen et al., Cancer Treat. Rev. 21(3):215-245 (1995)). As such, there is significant interest in identifying and characterizing novel polypeptides having structural and functional similarity to the tetranectin protein.

We herein describe the identification and characterization of novel polypeptides having homology to tetranectin protein, designated herein as PRO1345 polypeptides.

127. **PRO1245**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1245 polypeptides.

128. **PRO358**

Serine protease inhibitors are of interest because they inhibit catabolism and are sometimes associated with regeneration of tissue. For example, a gene encoding a plasma protein associated with liver regeneration has been cloned and termed regeneration-associated serpin-1 (RASP-1). New, et al., Biochem. Biophys. Res. Commun., 223(2):404-412 (1996). While serine protease inhibitors are of interest, particularly of interest are those which have sequence identity with known serine protease inhibitors such as RASP-1.

We herein describe the identification and characterization of novel polypeptides having homology to RASP-1, designated herein as PRO1245 polypeptides.

129. PRO1195

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1195 polypeptides.

130. PRO1270

The recognition of carbohydrates by lectins has been found to play an important role in various aspects of eukaryotic physiology. A number of different animal and plant lectin families exist, but it is the calcium dependent, or type C, lectins that have recently garnered the most attention. For example, the recognition of carbohydrate residues on either endothelial cells or leukocytes by the selectin family of calcium dependent lectins has been found to be of profound importance to the trafficking of leukocytes to inflammatory sites. Lasky, L., Ann. Rev. Biochem., 64 113-139 (1995). The biophysical analysis of these adhesive interactions has suggested that lectin-carbohydrate binding evolved in this case to allow for the adhesion between leukocytes and the endothelium under the high shear conditions of the vasculature. Thus, the rapid on rates of carbohydrate recognition by such lectins allows for a hasty acquisition of ligand, a necessity under the high shear of the vascular flow. The physiological use of type C lectins in this case is also supported by the relatively low affinities of these interactions, a requirement for the leukocyte rolling phenomenon that has been observed to occur at sites of acute inflammation. The crystal structures of the mannose binding protein (Weis *et al.*, Science 254, 1608-1615 [1991]; Weis *et al.*, Nature 360 127-134 [1992]) and E-selectin (Graves *et al.*, Nature 367(6463), 532-538 [1994]), together with various mutagenesis analyses (Erbe *et al.*, J. Cell. Biol. 119(1), 215-227 [1992]; Drickamer, Nature 360, 183-186 [1992]; Iobst *et al.*, J. Biol. Chem. 169(22), 15505-15511 [1994]; Kogan *et al.*, J. Biol. Chem. 270(23), 14047-14055 [1995]), is consistent with the supposition that the type C lectins are, in general, involved with the rapid recognition of clustered carbohydrates. Together, these data suggest that type C lectins perform a number of critical physiological phenomena through the rapid, relatively low affinity recognition of carbohydrates.

Given the obvious importance of the lectin proteins in numerous biological processes, efforts are currently being made to identify novel lectin proteins or proteins having sequence homology to lectin proteins. We herein describe the identification and characterization of novel polypeptides having homology to a lectin protein, designated herein as PRO1270 polypeptides.

131. PRO1271

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and

characterization of novel transmembrane polypeptides, designated herein as PRO1271 polypeptides.

132. **PRO1375**

The proteins L1CAM, G6PD and P55 are each associated with various known disease states. Thus, the genomic loci of Fugu rubripes homologs of the human disease genes L1CAM, G6PD and P55 were analyzed. This analysis led to the the identification of putative protein 2 (PUT2), GENBANK locus AF026198, accession AF026198. (See GENBANK submission data). Thus, PUT2 and proteins which have sequence identity with PUT2, are of interest.

133. **PRO1385**

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of novel secreted polypeptides, designated herein as PRO1385 polypeptides.

134. **PRO1387**

Membrane-bound proteins of myelin are of interest because of their possible implications in various nervous system disorders associated with improper myelination. Myelin is a cellular sheath, formed by glial cells, that surrounds axons and axonal processes that enhances various electrochemical properties and provides trophic support to the neuron. Myelin is formed by Schwann cells in the peripheral nervous system (PNS) and by oligodendrocytes in the central nervous system (CNS). Improper myelination of central and peripheral neurons occurs in a number of pathologies and leads to improper signal conduction within the nervous systems. Among the various demyelinating diseases Multiple Sclerosis is the most notable.

The predominant integral membrane protein of the CNS myelin of amphibians, reptiles, birds and mammals are proteolipid protein (PLP) and P0, the main glycoprotein in PNS myelin. (Schlieess and Stoffel, Biol. Chem. Hoppe Seyler (1991) 372(9):865-874). In view of the importance of membrane-bound proteins of the myelin, efforts are being undertaken by both industry and academia to identify and characterize various myelin proteins (see Stratmann and Jeserich, J. Neurochem (1995) 64(6):2427-2436).

We herein describe the identification and characterization of novel polypeptides having homology to myelin protein, designated herein as PRO1387 polypeptides.

135. **PRO1384**

One class of receptor proteins that has been of interest is the NKG2 family of type II transmembrane molecules that are expressed in natural killer cells. These proteins, which have been shown to be covalently associated with CD94, are involved in natural killer cell-mediated recognition of different HLA-allotypes (Plougastel, B. *et al., Eur. J. Immunol.* (1997) 27(11):2835-2839), and interact with major histocompatibility complex (MHC) class I to either inhibit or activate functional activity (Ho, EL. *et al., Proc. Natl. Acad. Sci.* (1998) 95(11):6320-6325). Accordingly, the identification and characterization of new members of this family

of receptor proteins is of interest (see Houchins JP, *et al. J. Exp. Med.* (1991) 173(4):1017-1020).

SUMMARY OF THE INVENTION

1. PRO281

A cDNA clone (DNA16422-1209) has been identified, having homology to nucleic acid encoding testis enhanced gene transcript (TEGT) protein that encodes a novel polypeptide, designated in the present application as "PRO281".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO281 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO281 polypeptide having the sequence of amino acid residues from about 1 or about 15 to about 345, inclusive of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO281 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 80 or about 122 and about 1114, inclusive, of Figure 1 (SEQ ID NO:1). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209929 (DNA16422-1209) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209929 (DNA16422-1209).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 15 to about 345, inclusive of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO281 polypeptide having the sequence of amino acid residues from 1 or about 15 to about 345, inclusive of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO281 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 14 in the sequence of Figure 2 (SEQ ID NO:2). The multiple transmembrane domains have been tentatively identified as extending from about amino acid position 83 to about amino acid position 105, from about amino acid position 126 to about amino acid position 146, from about amino acid position 158 to about amino acid position 177, from about amino acid position 197 to about amino acid position 216, from about amino acid position 218 to about amino acid position 238, from about amino acid position 245 to about amino acid position 265, and from about amino acid position 271 to about amino acid position 290 in the PRO281 amino acid sequence (Figure 2, SEQ ID NO:2).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 15 to about 345, inclusive of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO281 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 1 (SEQ ID NO:1).

In another embodiment, the invention provides isolated PRO281 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO281 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 15 to about 345 of Figure 2 (SEQ ID NO:2).

In another aspect, the invention concerns an isolated PRO281 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 15 to about 345, inclusive of Figure 2 (SEQ ID NO:2).

In a further aspect, the invention concerns an isolated PRO281 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 15 to about 345, inclusive of Figure 2 (SEQ ID NO:2).

In yet another aspect, the invention concerns an isolated PRO281 polypeptide, comprising the sequence of amino acid residues 1 or about 15 to about 345, inclusive of Figure 2 (SEQ ID NO:2), or a fragment thereof sufficient to provide a binding site for an anti-PRO281 antibody. Preferably, the PRO281 fragment retains a qualitative biological activity of a native PRO281 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO281 polypeptide having the sequence of amino acid residues from about 1 or about 15 to about 345, inclusive of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO281 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO281 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO281 polypeptide by contacting the native PRO281 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO281 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

2. **PRO276**

A cDNA clone (DNA16435-1208) has been identified that encodes a novel polypeptide having two transmembrane domains and designated in the present application as "PRO276."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO276 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO276 polypeptide having the sequence of amino acid residues from about 1 to about 251, inclusive of Figure 4 (SEQ ID NO:6), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO276 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 180 and about 932, inclusive, of Figure 3 (SEQ ID NO:5). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209930 (DNA16435-1208), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209930 (DNA16435-1208).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 251, inclusive of Figure 4 (SEQ ID NO:6), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO276 polypeptide having the sequence of amino acid residues from about 1 to about 251, inclusive of Figure 4 (SEQ ID NO:6), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO276 polypeptide in its soluble, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains are at about amino acds 98-116 and 152-172.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 251, inclusive of Figure 4 (SEQ ID NO:6), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO276 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO276 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO276 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 251 of Figure 4 (SEQ ID NO:6).

In another aspect, the invention concerns an isolated PRO276 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 251, inclusive of Figure 4 (SEQ ID NO:6).

In a further aspect, the invention concerns an isolated PRO276 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 through 251 of Figure 4 (SEQ ID NO:6).

In yet another aspect, the invention concerns an isolated PRO276 polypeptide, comprising the sequence of amino acid residues 1 to about 251, inclusive of Figure 4 (SEQ ID NO:6), or a fragment thereof sufficient to provide a binding site for an anti-PRO276 antibody. Preferably, the PRO276 fragment retains a qualitative biological activity of a native PRO276 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO276 polypeptide having the sequence of amino acid residues from about 1 to about 251, inclusive of Figure 4 (SEQ ID NO:6), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO276 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO276 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO276 polypeptide, by contacting the native PRO276 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO276 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

3. **PRO189**

A cDNA clone (DNA21624-1391) has been identified that encodes a novel polypeptide, designated in the present application as "PRO189". PRO189 polypeptides have a cytosolic fatty-acid binding domain.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO189 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO189 polypeptide having the sequence of amino acid residues from about 1 to about 367, inclusive of Figure 6 (SEQ ID NO:8), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO189 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 200 and about 1300, inclusive, of Figure 5 (SEQ ID NO:7). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209917

(DNA21624-1391), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209917 (DNA21624-1391).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 367, inclusive of Figure 6 (SEQ ID NO:8), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO189 polypeptide having the sequence of amino acid residues from about 1 to about 367, inclusive of Figure 6 (SEQ ID NO:8), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 367, inclusive of Figure 6 (SEQ ID NO:8), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO189 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO189 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 367 of Figure 6 (SEQ ID NO:8).

In another aspect, the invention concerns an isolated PRO189 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 367, inclusive of Figure 6 (SEQ ID NO:8).

In a further aspect, the invention concerns an isolated PRO189 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 through 367 of Figure 6 (SEQ ID NO:8).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO189 polypeptide having the sequence of amino acid residues from about 1 to about 367, inclusive of Figure 6 (SEQ ID NO:8), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising

the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO189 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO189 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO189 polypeptide, by contacting the native PRO189 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO189 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

4. **PRO190**

Applicants have identified a cDNA clone that encodes a novel polypeptide having seven transmembrane domains and having sequence identity with CMP-sialic acid and UDP-galactose transporters, wherein the polypeptide is designated in the present application as "PRO190".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO190 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO190 polypeptide having amino acid residues 1 through 424 of Figure 9 (SEQ ID NO:14), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on June 2, 1998 with the ATCC as DNA23334-1392 which includes the nucleotide sequence encoding PRO190.

In another embodiment, the invention provides isolated PRO190 polypeptide. In particular, the invention provides isolated native sequence PRO190 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 424 of Figure 9 (SEQ ID NO:14). An additional embodiment of the present invention is directed to an isolated PRO190 polypeptide, excluding the transmembrane domains. Optionally, the PRO190 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on June 2, 1998 with the ATCC as DNA23334-1392.

In another embodiment, the invention provides an expressed sequence tag (EST) comprising the nucleotide sequence of SEQ ID NO:15.

5. **PRO341**

A cDNA clone (DNA26288-1239) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO341".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO341 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO341 polypeptide having

the sequence of amino acid residues from about 1 or about 18 to about 458, inclusive of Figure 12 (SEQ ID NO:20), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO341 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 380 or about 431 and about 1753, inclusive, of Figure 11 (SEQ ID NO:19). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209792 (DNA26288-1239) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209792 (DNA26288-1239).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 458, inclusive of Figure 12 (SEQ ID NO:20), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 165 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO341 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 458, inclusive of Figure 12 (SEQ ID NO:20), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO341 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 17 in the sequence of Figure 12 (SEQ ID NO:20). The transmembrane domains have been tentatively identified as extending from about amino acid position 171 to about amino acid position 190, from about amino acid position 220 to about amino acid position 239, from about amino acid position 259 to about amino acid position 275, from about amino acid position 286 to about amino acid position 305, from about amino acid position 316 to about amino acid position 335, from about amino acid position 353 to about amino acid position 378 and from about amino acid position 396 to about amino acid position 417 in the PRO341 amino acid sequence (Figure 12, SEQ ID NO:20).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more

preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 458, inclusive of Figure 12 (SEQ ID NO:20), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO341 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 11 (SEQ ID NO:19).

In another embodiment, the invention provides isolated PRO341 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO341 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 18 to about 458 of Figure 12 (SEQ ID NO:20).

In another aspect, the invention concerns an isolated PRO341 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 458, inclusive of Figure 12 (SEQ ID NO:20).

In a further aspect, the invention concerns an isolated PRO341 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 458, inclusive of Figure 12 (SEQ ID NO:20).

In yet another aspect, the invention concerns an isolated PRO341 polypeptide, comprising the sequence of amino acid residues 1 or about 18 to about 458, inclusive of Figure 12 (SEQ ID NO:20), or a fragment thereof sufficient to provide a binding site for an anti-PRO341 antibody. Preferably, the PRO341 fragment retains a qualitative biological activity of a native PRO341 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO341 polypeptide having the sequence of amino acid residues from about 1 or about 18 to about 458, inclusive of Figure 12 (SEQ ID NO:20), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA12920 comprising the nucleotide sequence of SEQ ID NO:21 (see Figure 13).

6. **PRO180**

A cDNA clone (DNA26843-1389) has been identified that encodes a novel polypeptide having multiple transmembrane domains designated in the present application as "PRO180".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO180 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO180 polypeptide having the sequence of amino acid residues from about 1 to about 266, inclusive of Figure 15 (SEQ ID NO:23), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO180 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 121 and about 918, inclusive, of Figure 14 (SEQ ID NO:22). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203099 (DNA26843-1389), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203099 (DNA26843-1389).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 266, inclusive of Figure 15 (SEQ ID NO:23), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO180 polypeptide having the sequence of amino acid residues from about 1 to about 266, inclusive of Figure 15 (SEQ ID NO:23), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO180 polypeptide in its soluble form, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains are shown in Figure 15. It is believed that PRO180 has a type II transmembrane domain from about amino acids 13-33 of SEQ ID NO:23.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 266, inclusive of Figure 15 (SEQ ID NO:23), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO180 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO180 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO180 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 266 of Figure 15 (SEQ ID NO:23).

In another aspect, the invention concerns an isolated PRO180 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 266, inclusive of Figure 15 (SEQ ID NO:23).

In a further aspect, the invention concerns an isolated PRO180 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 through 266 of Figure 15 (SEQ ID NO:23).

In yet another aspect, the invention concerns an isolated PRO180 polypeptide, comprising the sequence of amino acid residues 1 to about 266, inclusive of Figure 15 (SEQ ID NO:23), or a fragment thereof sufficient to provide a binding site for an anti-PRO180 antibody. Preferably, the PRO180 fragment retains a qualitative biological activity of a native PRO180 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO180 polypeptide having the sequence of amino acid residues from about 1 to about 266, inclusive of Figure 15 (SEQ ID NO:23), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO180 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO180 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO180 polypeptide, by contacting the native PRO180 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO180 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

In another embodiment, the invention provides an expressed sequence tag (EST) (DNA12922) comprising the nucleotide sequence of Figure 16 (SEQ ID NO:24).

7. **PRO194**

Applicants have identified a cDNA clone that encodes a novel transmembrane polypeptide, wherein the polypeptide is designated in the present application as "PRO194".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO194 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO194 polypeptide having amino acid residues 1 to 264 of Figure 18 (SEQ ID NO:28), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO194 polypeptide having amino acid residues about 18 to 264 of Figure 18 (SEQ ID NO:28) or amino acid 1 or about 18 to X of Figure 18 (SEQ ID NO:28), where X is any amino acid from 96 to 105 of Figure 18 (SEQ ID NO:28), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA26844-1394 vector deposited on June 2, 1998 as ATCC 209926 which includes the nucleotide sequence encoding PRO194.

In another embodiment, the invention provides isolated PRO194 polypeptide. In particular, the invention provides isolated native sequence PRO194 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 264 of Figure 18 (SEQ ID NO:28). Additional embodiments of the present invention are directed to PRO194 polypeptides comprising amino acids about 18 to 264 of Figure 18 (SEQ ID NO:28) or amino acid 1 or about 18 to X of Figure 18 (SEQ ID NO:28), where X is any amino acid from 96 to 105 of Figure 18 (SEQ ID NO:28). Optionally, the PRO194 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA26844-1394 vector deposited on June 2, 1998 as ATCC 209926.

8. **PRO203**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity to glutathione-S-transferase, wherein the polypeptide is designated in the present application as "PRO203".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO203 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO203 polypeptide having amino acid residues 1 to 347 of Figure 20 (SEQ ID NO:30), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO203 polypeptide having amino acid residues X to 347 of Figure 20 (SEQ ID NO:30), where X is any amino acid from 83 to 92 of Figure 20 (SEQ ID NO:30), or is complementary to such encoding nucleic acid sequence, and

remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA30862-1396 vector deposited on June 2, 1998, as ATCC 209920 which includes the nucleotide sequence encoding PRO203.

In another embodiment, the invention provides isolated PRO203 polypeptide. In particular, the invention provides isolated native sequence PRO203 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 347 of Figure 20 (SEQ ID NO:30). Additional embodiments of the present invention are directed to PRO203 polypeptides comprising amino acid X to 347 of Figure 20 (SEQ ID NO:30), where X is any amino acid from 83 to 92 of Figure 20 (SEQ ID NO:30). Optionally, the PRO203 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA30862-1396 vector deposited on June 2, 1998, as ATCC 209920.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA15618 which comprises the nucleotide sequence of Figure 21 (SEQ ID NO:31).

9. PRO290

A cDNA clone (DNA35680-1212) has been identified which encodes a polypeptide designated in the present application as "PRO290." PRO290 polypeptides have sequence identity with NTII-1, FAN and beige.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO290 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO290 polypeptide having the sequence of amino acid residues from about 1 to about 1003, inclusive of Figure 23 (SEQ ID NO:33), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO290 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 293 and about 3301, inclusive, of Figure 22 (SEQ ID NO:32). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209790 (DNA35680-1212), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209790 (DNA35680-1212).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 1003, inclusive of Figure 23 (SEQ ID

NO:33), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO290 polypeptide having the sequence of amino acid residues from about 1 to about 1003, inclusive of Figure 23 (SEQ ID NO:33), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 1003, inclusive of Figure 23 (SEQ ID NO:33), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO290 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO290 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 1003 of Figure 23 (SEQ ID NO:33).

In another aspect, the invention concerns an isolated PRO290 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 1003, inclusive of Figure 23 (SEQ ID NO:33).

In a further aspect, the invention concerns an isolated PRO290 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 through 1003 of Figure 23 (SEQ ID NO:33).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO290 polypeptide having the sequence of amino acid residues from about 1 to about 1003, inclusive of Figure 23 (SEQ ID NO:33), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO290 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO290 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO290 polypeptide, by contacting the native PRO290 polypeptide with a candidate molecule and

monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO290 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

10. PRO874

Applicants have identified a cDNA clone that encodes a novel multi-span transmembrane polypeptide, which is designated in the present application as "PRO874".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO874 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO874 polypeptide having amino acid residues 1 to 321 of Figure 25 (SEQ ID NO:36), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO874 polypeptide having amino acid from about X to 321 of Figure 25 (SEQ ID NO:36), where X is any amino acid from about 270 to about 279 of Figure 25 (SEQ ID NO:36), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA40621-1440 vector deposited on June 2, 1998, as ATCC 209922 which includes the nucleotide sequence encoding PRO874.

In another embodiment, the invention provides isolated PRO874 polypeptide. In particular, the invention provides isolated native sequence PRO874 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 321 of Figure 25 (SEQ ID NO:36). Additional embodiments of the present invention are directed to PRO874 polypeptides comprising amino acids X to 321 of Figure 25 (SEQ ID NO:36), where X is any amino acid from about 270 to about 279 of Figure 25 (SEQ ID NO:36). Optionally, the PRO874 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA40621-1440 vector deposited on June 2, 1998, as ATCC 209922.

11. PRO710

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to CDC45 protein, wherein the polypeptide is designated in the present application as "PRO710".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO710 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO710 polypeptide having amino acid residues 1 to 566 of Figure 27 (SEQ ID NO:41), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO710 polypeptide having amino acid residues about 33 to 566 of Figure 27 (SEQ ID NO:41) or amino acid 1 or about 33 to X of Figure 27 (SEQ ID NO:41), where X is any amino acid from 449 to 458 of Figure 27 (SEQ ID NO:41), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA44161-1434 vector deposited on May 27, 1998 as ATCC 209907 which

includes the nucleotide sequence encoding PRO710.

In another embodiment, the invention provides isolated PRO710 polypeptide. In particular, the invention provides isolated native sequence PRO710 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 566 of Figure 27 (SEQ ID NO:41). Additional embodiments of the present invention are directed to PRO710 polypeptides comprising amino acids about 33 to 566 of Figure 27 (SEQ ID NO:41) or amino acid 1 or about 33 to X of Figure 27 (SEQ ID NO:41), where X is any amino acid from 449 to 458 of Figure 27 (SEQ ID NO:41). Optionally, the PRO710 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA44161-1434 vector deposited on May 27, 1998 as ATCC 209907.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA38190 comprising the nucleotide sequence of Figure 28 (SEQ ID NO:42).

12. PRO1151

A cDNA clone (DNA44694-1500) has been identified, having homology to nucleic acid encoding C1q protein, that encodes a novel polypeptide, designated in the present application as "PRO1151".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1151 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1151 polypeptide having the sequence of amino acid residues from about 1 or about 21 to about 259, inclusive of Figure 30 (SEQ ID NO:47), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1151 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 272 or about 332 and about 1048, inclusive, of Figure 29 (SEQ ID NO:46). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203114 (DNA44694-1500) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203114 (DNA44694-1500).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 21 to about 259, inclusive of Figure 30 (SEQ ID NO:47), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1151 polypeptide having the sequence of amino acid residues from 1 or about 21 to about 259, inclusive of Figure 30 (SEQ ID NO:47), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1151 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 20 in the sequence of Figure 30 (SEQ ID NO:47).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 21 to about 259, inclusive of Figure 30 (SEQ ID NO:47), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1151 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 29 (SEQ ID NO:46).

In another embodiment, the invention provides isolated PRO1151 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1151 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 21 to about 259 of Figure 30 (SEQ ID NO:47).

In another aspect, the invention concerns an isolated PRO1151 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 21 to about 259, inclusive of Figure 30 (SEQ ID NO:47).

In a further aspect, the invention concerns an isolated PRO1151 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 21 to about 259, inclusive of Figure 30 (SEQ ID NO:47).

In yet another aspect, the invention concerns an isolated PRO1151 polypeptide, comprising the sequence of amino acid residues 1 or about 21 to about 259, inclusive of Figure 30 (SEQ ID NO:47), or a fragment thereof sufficient to provide a binding site for an anti-PRO1151 antibody. Preferably, the PRO1151 fragment

retains a qualitative biological activity of a native PRO1151 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1151 polypeptide having the sequence of amino acid residues from about 1 or about 21 to about 259, inclusive of Figure 30 (SEQ ID NO:47), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1151 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1151 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1151 polypeptide by contacting the native PRO1151 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1151 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

13. **PRO1282**

A cDNA clone (DNA45495-1550) has been identified that encodes a novel polypeptide having sequence identity with leucine rich repeat proteins and designated in the present application as "PRO1282."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1282 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1282 polypeptide having the sequence of amino acid residues from about 24 to about 673, inclusive of Figure 32 (SEQ ID NO:52), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1282 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 189 and about 2138, inclusive, of Figure 31 (SEQ ID NO:51). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203156 (DNA45495-1550), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203156 (DNA45495-1550).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 24 to about 673, inclusive of Figure 32 (SEQ ID NO:52), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1282 polypeptide having the sequence of amino acid residues from about 24 to about 673, inclusive of Figure 32 (SEQ ID NO:52), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1282 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 23 in the sequence of Figure 32 (SEQ ID NO:52). The transmembrane domain has been tentatively identified as extending from about amino acid position 579 through about amino acid position 599 in the PRO1282 amino acid sequence (Figure 32, SEQ ID NO:52).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 24 to about 673, inclusive of Figure 32 (SEQ ID NO:52), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1282 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1282 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1282 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 24 through 673 of Figure 32 (SEQ ID NO:52).

In another aspect, the invention concerns an isolated PRO1282 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 24 to about 673, inclusive of Figure 32 (SEQ ID NO:52).

In a further aspect, the invention concerns an isolated PRO1282 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 24 through 673 of Figure 32 (SEQ ID NO:52).

In yet another aspect, the invention concerns an isolated PRO1282 polypeptide, comprising the sequence of amino acid residues 24 to about 673, inclusive of Figure 32 (SEQ ID NO:52), or a fragment thereof sufficient to provide a binding site for an anti-PRO1282 antibody. Preferably, the PRO1282 fragment retains a qualitative biological activity of a native PRO1282 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1282 polypeptide having the sequence of amino acid residues from about 24 to about 673, inclusive of Figure 32 (SEQ ID NO:52), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1282 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1282 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1282 polypeptide, by contacting the native PRO1282 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1282 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

14. <u>PRO358</u>

Applicants have identified a novel cDNA clone that encodes novel human Toll polypeptides, designated in the present application as PRO358.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising a DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO358 polypeptide having amino acids 20 to 575 of Figure 34 (SEQ ID NO:57), or (b) the complement of the DNA molecule of (a). The complementary DNA molecule preferably remains stably bound to such encoding nucleic acid sequence under at least moderate, and optionally, under high stringency conditions.

In a further embodiment, the isolated nucleic acid molecule comprises a polynucleotide that has at least about 90%, preferably at least about 95% sequence identity with a polynucleotide encoding a polypeptide comprising the sequence of amino acids 1 to 811 of Figure 34 (SEQ ID NO:57).

In a specific embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding native or variant PRO358 polypeptide, with or without the N-terminal signal sequence, and with or without the transmembrane regions of the respective full-length sequences. In one aspect, the isolated nucleic acid comprises DNA encoding a mature, full-length native PRO358 polypeptide having amino acid residues 1 to 811 of Figure 34 (SEQ ID NO:57), or is complementary to such encoding nucleic acid sequence. In another aspect, the invention concerns an isolated nucleic acid molecule that comprises DNA encoding a native PRO358 polypeptide without an N-terminal signal sequence, or is complementary to such encoding nucleic acid sequence. In yet another embodiment, the invention concerns nucleic acid encoding transmembrane-domain deleted or inactivated forms of the full-length native PRO358 protein.

In another embodiment, the invention provides an isolated nucleic acid molecule which comprises the clone (DNA 47361-1249) deposited on November 7, 1997, under ATCC number 209431.

In a specific embodiment, the invention provides a vector comprising a polynucleotide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity with a polynucleotide encoding a polypeptide comprising the sequence of amino acids 20 to 811 of Figure 34 (SEQ ID NO:57), or the complement of such polynucleotide. In a particular embodiment, the vector comprises DNA encoding the novel Toll homologue (PRO358), with or without the N-terminal signal sequence (about amino acids 1 to 19), or a transmembrane-domain (about amino acids 576-595) deleted or inactivated variant thereof, or the extracellular domain (about amino acids 20 to 595) of the mature protein, or a protein comprising any one of these sequences. A host cell comprising such a vector is also provided.

In another embodiment, the invention provides isolated PRO358 polypeptides. The invention further provides an isolated native sequence PRO358 polypeptide, or variants thereof. In particular, the invention provides an isolated native sequence PRO358 polypeptide, which in certain embodiments, includes the amino acid sequence comprising residues 20 to 575, or 20 to 811, or 1 to 811 of Figure 34 (SEQ ID NO:57).

In yet another embodiment, the invention concerns agonists and antagonists of the native PRO358 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO358 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of the native PRO358 polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO358 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

The invention further concerns a composition comprising an antibody specifically binding a PRO358 polypeptide, in combination with a pharmaceutically acceptable carrier.

The invention also concerns a method of treating septic shock comprising administering to a patient an effective amount of an antagonist of a PRO358 polypeptide. In a specific embodiment, the antagonist is a blocking antibody specifically binding a native PRO358 polypeptide.

15. **PRO1310**

A cDNA clone (DNA47394-1572) has been identified that encodes a novel polypeptide having sequence identity with carboxypeptidase X2 and designated in the present application as "PRO1310."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1310 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1310 polypeptide having the sequence of amino acid residues from about 26 to about 765, inclusive of Figure 36 (SEQ ID NO:62), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1310 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 401 and about 2593, inclusive, of Figures 35A-B (SEQ ID NO:61). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203109 (DNA47394-1572), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203109 (DNA47394-1572).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 26 to about 765, inclusive of Figure 36 (SEQ ID NO:62), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1310 polypeptide having the sequence of amino acid residues from about 26 to about 765, inclusive of Figure 36 (SEQ ID NO:62), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 26 to about 765, inclusive of Figure 36 (SEQ ID NO:62), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1310 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1310 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 26 through 765 of Figure 36 (SEQ ID NO:62).

In another aspect, the invention concerns an isolated PRO1310 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 26 to about 765, inclusive of Figure 36 (SEQ ID NO:62).

In a further aspect, the invention concerns an isolated PRO1310 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 26 through 765 of Figure 36 (SEQ ID NO:62).

In yet another aspect, the invention concerns an isolated PRO1310 polypeptide, comprising the sequence of amino acid residues 26 to about 765, inclusive of Figure 36 (SEQ ID NO:62), or a fragment thereof sufficient to provide a binding site for an anti-PRO1310 antibody. Preferably, the PRO1310 fragment retains a qualitative biological activity of a native PRO1310 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1310 polypeptide having the sequence of amino acid residues from about 26 to about 765, inclusive of Figure 36 (SEQ ID NO:62), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1310 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1310 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1310 polypeptide, by contacting the native PRO1310 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1310 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

16. **PRO698**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to olfactomedin, wherein the polypeptide is designated in the present application as "PRO698".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO698 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO698

polypeptide having amino acid residues 1 to 510 of Figure 38 (SEQ ID NO:67), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO698 polypeptide having amino acid residues about 21 to 510 of Figure 38 (SEQ ID NO:67), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA48320-1433 vector deposited on May 27, 1998 as ATCC 209904 which includes the nucleotide sequence encoding PRO698.

In another embodiment, the invention provides isolated PRO698 polypeptide. In particular, the invention provides isolated native sequence PRO698 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 510 of Figure 38 (SEQ ID NO:67). Additional embodiments of the present invention are directed to PRO698 polypeptides comprising amino acids about 21 to 510 of Figure 38 (SEQ ID NO:67). Optionally, the PRO698 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA48320-1433 vector deposited on May 27, 1998 as ATCC 209904.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA39906 comprising the nucleotide sequence of Figure 39 (SEQ ID NO:68).

17. **PRO732**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to the human placental protein Diff33, wherein the polypeptide is designated in the present application as "PRO732".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO732 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO732 polypeptide having amino acid residues 1 to 453 of Figure 41 (SEQ ID NO:73), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO732 polypeptide having amino acid residues about 29 to 453 of Figure 41 (SEQ ID NO:73) or amino acid 1 or about 29 to X of Figure 41 (SEQ ID NO:73), where X is any amino acid from 31 to 40 of Figure 41 (SEQ ID NO:73), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA48334-1435 vector deposited on June 2, 1998 as ATCC 209924 which includes the nucleotide sequence encoding PRO732.

In another embodiment, the invention provides isolated PRO732 polypeptide. In particular, the invention provides isolated native sequence PRO732 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 453 of Figure 41 (SEQ ID NO:73). Additional embodiments of the present invention are directed to PRO732 polypeptides comprising amino acids about 29 to 453 of Figure 41 (SEQ ID NO:73) or amino acid 1 or about 29 to X of Figure 41 (SEQ ID NO:73), where X is any amino acid from 31 to 40 of Figure 41 (SEQ ID NO:73). Optionally, the PRO732 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA48334-1435 vector deposited on June 2,

1998 as ATCC 209924.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA20239 comprising the nucleotide sequence of Figure 42 (SEQ ID NO:74).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA38050 comprising the nucleotide sequence of Figure 43 (SEQ ID NO:75).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA40683 comprising the nucleotide sequence of Figure 44 (SEQ ID NO:76).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA42580 comprising the nucleotide sequence of Figure 45 (SEQ ID NO:77).

18. **PRO1120**

A cDNA clone (DNA48606-1479) has been identified that encodes a novel polypeptide having homology sulfatases, designated in the present application as "PRO1120."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1120 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1120 polypeptide having the sequence of amino acid residues from about 18 to about 867, inclusive of Figure 47 (SEQ ID NO:84), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1120 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 659 and about 3208, inclusive, of Figures 46A-B (SEQ ID NO:83). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203040 (DNA48606-1479), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203040 (DNA48606-1479).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 18 to about 867, inclusive of Figure 47 (SEQ ID NO:84), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under

stringent conditions with (a) a DNA molecule encoding a PRO1120 polypeptide having the sequence of amino acid residues from about 18 to about 867, inclusive of Figure 47 (SEQ ID NO:84), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1120 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 17 in the sequence of Figure 47 (SEQ ID NO:84).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to about 867, inclusive of Figure 47 (SEQ ID NO:84), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1120 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1120 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1120 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 18 to 867 of Figure 47 (SEQ ID NO:84).

In another aspect, the invention concerns an isolated PRO1120 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 18 to about 867, inclusive of Figure 47 (SEQ ID NO:84).

In a further aspect, the invention concerns an isolated PRO1120 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to 867 of Figure 47 (SEQ ID NO:84).

In yet another aspect, the invention concerns an isolated PRO1120 polypeptide, comprising the sequence of amino acid residues 18 to about 867, inclusive of Figure 47 (SEQ ID NO:84), or a fragment thereof sufficient to provide a binding site for an anti-PRO1120 antibody. Preferably, the PRO1120 fragment retains a qualitative biological activity of a native PRO1120 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1 120 polypeptide having the sequence of amino acid residues from about 18 to about 867, inclusive of Figure 47 (SEQ ID NO:84), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1120 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1120 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1120 polypeptide, by contacting the native PRO1120 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1120 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

19. **PRO537**

A cDNA clone (DNA49141-1431) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO537".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO537 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO537 polypeptide having the sequence of amino acid residues from about 1 or about 32 to about 115, inclusive of Figure 49 (SEQ ID NO:95), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO537 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 97 or about 190 and about 441, inclusive, of Figure 48 (SEQ ID NO:94). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203003 (DNA49141-1431) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203003 (DNA49141-1431).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 32 to about 115, inclusive of Figure 49 (SEQ ID NO:95), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO537 polypeptide having the sequence of amino acid residues from 1 or about 32 to about 115, inclusive of Figure 49 (SEQ ID NO:95), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO537 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 31 in the sequence of Figure 49 (SEQ ID NO:95).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 32 to about 115, inclusive of Figure 49 (SEQ ID NO:95), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO537 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 48 (SEQ ID NO:94).

In another embodiment, the invention provides isolated PRO537 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO537 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 32 to about 115 of Figure 49 (SEQ ID NO:95).

In another aspect, the invention concerns an isolated PRO537 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85 % sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95 % sequence identity to the sequence of amino acid residues 1 or about 32 to about 115, inclusive of Figure 49 (SEQ ID NO:95).

In a further aspect, the invention concerns an isolated PRO537 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 32 to about 115, inclusive of Figure 49 (SEQ ID NO:95).

In yet another aspect, the invention concerns an isolated PRO537 polypeptide, comprising the sequence of amino acid residues 1 or about 32 to about 115, inclusive of Figure 49 (SEQ ID NO:95), or a fragment thereof sufficient to provide a binding site for an anti-PRO537 antibody. Preferably, the PRO537 fragment

retains a qualitative biological activity of a native PRO537 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO537 polypeptide having the sequence of amino acid residues from about 1 or about 32 to about 115, inclusive of Figure 49 (SEQ ID NO:95), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

20. **PRO536**

A cDNA clone (DNA49142-1430) has been identified, that encodes a novel secreted polypeptide, designated in the present application as "PRO536".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO536 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO536 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 313, inclusive of Figure 51 (SEQ ID NO:97), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO536 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 48 or about 123 and about 986, inclusive, of Figure 50 (SEQ ID NO:96). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203002 (DNA49142-1430) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203002 (DNA49142-1430).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 313, inclusive of Figure 51 (SEQ ID NO:97), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA

molecule encoding a PRO536 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 313, inclusive of Figure 51 (SEQ ID NO:97), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO536 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 25 in the sequence of Figure 51 (SEQ ID NO:97).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 313, inclusive of Figure 51 (SEQ ID NO:97), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO536 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 50 (SEQ ID NO:96).

In another embodiment, the invention provides isolated PRO536 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO536 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 26 to about 313 of Figure 51 (SEQ ID NO:97).

In another aspect, the invention concerns an isolated PRO536 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 313, inclusive of Figure 51 (SEQ ID NO:97).

In a further aspect, the invention concerns an isolated PRO536 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 313, inclusive of Figure 51 (SEQ ID NO:97).

In yet another aspect, the invention concerns an isolated PRO536 polypeptide, comprising the sequence of amino acid residues 1 or about 26 to about 313, inclusive of Figure 51 (SEQ ID NO:97), or a fragment thereof sufficient to provide a binding site for an anti-PRO536 antibody. Preferably, the PRO536 fragment retains a qualitative biological activity of a native PRO536 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO536 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 313, inclusive of Figure 51 (SEQ ID NO:97), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

21. PRO535

A cDNA clone (DNA49143-1429) has been identified, having homology to nucleic acid encoding a putative peptidyl-prolyl isomerase that encodes a novel polypeptide, designated in the present application as "PRO535".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO535 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO535 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 201, inclusive of Figure 53 (SEQ ID NO:99), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO535 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 78 or about 153 and about 680, inclusive, of Figure 52 (SEQ ID NO:98). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203013 (DNA49143-1429) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203013 (DNA49143-1429).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 201, inclusive of Figure 53 (SEQ ID NO:99), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA

molecule encoding a PRO535 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 201, inclusive of Figure 53 (SEQ ID NO:99), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO535 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 25 in the sequence of Figure 53 (SEQ ID NO:99). The transmembrane domain has been tentatively identified as extending from about amino acid position 155 to about amino acid position 174 in the PRO535 amino acid sequence (Figure 53, SEQ ID NO:99).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 201, inclusive of Figure 53 (SEQ ID NO:99), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO535 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 52 (SEQ ID NO:98).

In another embodiment, the invention provides isolated PRO535 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO535 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 26 to about 201 of Figure 53 (SEQ ID NO:99).

In another aspect, the invention concerns an isolated PRO535 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 201, inclusive of Figure 53 (SEQ ID NO:99).

In a further aspect, the invention concerns an isolated PRO535 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 201, inclusive of Figure 53 (SEQ ID NO:99).

In yet another aspect, the invention concerns an isolated PRO535 polypeptide, comprising the sequence of amino acid residues 1 or about 26 to about 201, inclusive of Figure 53 (SEQ ID NO:99), or a fragment thereof sufficient to provide a binding site for an anti-PRO535 antibody. Preferably, the PRO535 fragment

retains a qualitative biological activity of a native PRO535 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO535 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 201, inclusive of Figure 53 (SEQ ID NO:99), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO535 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO535 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO535 polypeptide by contacting the native PRO535 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO535 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA30861 comprising the nucleotide sequence of Figure 54 (SEQ ID NO:100).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA36351 comprising the nucleotide sequence of Figure 55 (SEQ ID NO:101).

22. PRO718

Applicants have identified a cDNA clone that encodes a novel tetraspan membrane polypeptide, wherein the polypeptide is designated in the present application as "PRO718".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO718 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO718 polypeptide having amino acid residues 1 to 157 of Figure 57 (SEQ ID NO:103), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO718 polypeptide having amino acid residues X to 157 of Figure 57 (SEQ ID NO:103), where X is any amino acid from 143 to 152 of Figure 57 (SEQ ID NO:103), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA49647-1398 vector deposited on June 2, 1998 as ATCC 209919 which includes the nucleotide sequence encoding PRO718.

In another embodiment, the invention provides isolated PRO718 polypeptide. In particular, the invention provides isolated native sequence PRO718 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 157 of Figure 57 (SEQ ID NO:103). Additional embodiments of the present invention are directed to isolated PRO718 polypeptides comprising amino acids X to 157 of Figure 57

(SEQ ID NO:103), where X is any amino acid from 143 to 152 of Figure 57 (SEQ ID NO:103). Optionally, the PRO718 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA49647-1398 vector deposited on June 2, 1998 as ATCC 209919.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA15386 which comprises the nucleotide sequence of Figure 58 (SEQ ID NO:104).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA16630 which comprises the nucleotide sequence of Figure 59 (SEQ ID NO:105).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA16829 which comprises the nucleotide sequence of Figure 60 (SEQ ID NO:106).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA28357 which comprises the nucleotide sequence of Figure 61 (SEQ ID NO:107).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA43512 which comprises the nucleotide sequence of Figure 62 (SEQ ID NO:108).

23. **PRO872**

Applicants have identified a cDNA clone, DNA49819-1439, that encodes a novel polypeptide having homology to dehydrogenases wherein the polypeptide is designated in the present application as "PRO872".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO872 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO872 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 610, inclusive of Figure 64 (SEQ ID NO:113), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO872 polypeptide comprising DNA that hybridizes to the complement of the nucleic acid between about residues 68 and about 1843, inclusive of Figure 63 (SEQ ID NO:112). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209931 (DNA49819-1439), which was deposited on June 2, 1998. In a preferred embodiment, the nucleic acid comprises a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209931 (DNA49819-1439).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence

identity to the sequence of amino acid residues 1 or about 19 to about 610, inclusive of Figure 64 (SEQ ID NO:113).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO872 extracellular domain (ECD), with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble variants (i.e. transmembrane domain(s) deleted or inactivated) or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 to about amino acid position 18 in the sequence of Figure 64 (SEQ ID NO:113). The first transmembrane domain region has been tentatively identified as extending from about amino acid position 70 to about amino acid position 87 in the PRO872 amino acid sequence (Figure 64, SEQ ID NO:113).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 19 to about 610, inclusive of Figure 64 (SEQ ID NO:113).

Another embodiment is directed to fragments of a PRO872 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO872 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO872 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 19 to 610 of Figure 64 (SEQ ID NO:113).

In another aspect, the invention concerns an isolated PRO872 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 19 to 610, inclusive of Figure 64 (SEQ ID NO:113).

In a further aspect, the invention concerns an isolated PRO872 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 19 to 610 of Figure 64 (SEQ ID NO:113).

In another aspect, the invention concerns a PRO872 extracellular domain comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 19 to X of Figure 64 (SEQ ID NO:113), wherein X is any one of amino acid residues 66 to 75 of Figure 64 (SEQ ID NO:113).

In yet another aspect, the invention concerns an isolated PRO872 polypeptide, comprising the sequence of amino acid residues 1 or about 19 to about 610, inclusive of Figure 64 (SEQ ID NO:113), or a fragment thereof sufficient to provide a binding site for an anti-PRO872 antibody. Preferably, the PRO872 fragment

retains a qualitative biological activity of a native PRO872 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO872 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

In yet another embodiment, the invention concerns agonist and antagonists of the PRO872 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO872 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of a native PRO872 polypeptide.

In still a further embodiment, the invention concerns a composition comprising a PRO872 polypeptide as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

24. **PRO1063**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to human type IV collagenase, wherein the polypeptide is designated in the present application as "PRO1063".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1063 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1063 polypeptide having amino acid residues 1 to 301 of Figure 66 (SEQ ID NO:115), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO1063 polypeptide having amino acid residues about 22 to 301 of Figure 66 (SEQ ID NO:115), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA49820-1427 vector deposited on June 2, 1998 as ATCC 209932 which includes the nucleotide sequence encoding PRO1063.

In another embodiment, the invention provides isolated PRO1063 polypeptide. In particular, the invention provides isolated native sequence PRO1063 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 301 of Figure 66 (SEQ ID NO:115). Additional embodiments of the present invention are directed to PRO1063 polypeptides comprising amino acids about 22 to 301 of Figure 66 (SEQ ID NO:115). Optionally, the PRO1063 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA49820-1427 vector deposited on June 2, 1998 as ATCC 209932.

25. **PRO619**

A cDNA clone (DNA49821-1562) has been identified that encodes a novel polypeptide, designated in the present application as "PRO619." PRO619 polypeptides have sequence identity with VpreB genes, particularly to VpreB3.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO619 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO619 polypeptide having the sequence of amino acid residues from about 1 or 21 to about 123, inclusive of Figure 68 (SEQ ID NO:117), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO619 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 81 or 141 and about 449, inclusive, of Figure 67 (SEQ ID NO:116). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209981 (DNA49821-1562), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209981 (DNA49821-1562).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 21 to about 123, inclusive of Figure 68 (SEQ ID NO:117), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO619 polypeptide having the sequence of amino acid residues from about 1 or 21 to about 123, inclusive of Figure 68 (SEQ ID NO:117), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO619 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, which is in a soluble form. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 68 (SEQ ID NO:117).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 21 to about 123, inclusive of Figure 68 (SEQ ID NO:117), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO619 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 40 through about 80 nucleotides in length, preferably from about 20 through about 60 nucleotides in length, more preferably from about 20 through about 50 nucleotides in length, and most preferably from about 20 through about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO619 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO619 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 21 through 123 of Figure 68 (SEQ ID NO:117).

In another aspect, the invention concerns an isolated PRO619 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 21 through about 123, inclusive of Figure 68 (SEQ ID NO:117).

In a further aspect, the invention concerns an isolated PRO619 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 21 through 123 of Figure 68 (SEQ ID NO:117).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO619 polypeptide having the sequence of amino acid residues from about 1 or 21 to about 123, inclusive of Figure 68 (SEQ ID NO:117), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO619 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO619 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO619 polypeptide, by contacting the native PRO619 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO619 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

26. PRO943

A cDNA clone (DNA52192-1369) has been identified, having homology to nucleic acid encoding fibroblast growth factor receptor-4 that encodes a novel polypeptide, designated in the present application as "PRO943".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO943 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO943 polypeptide having the sequence of amino acid residues from about 1 or about 18 to about 504, inclusive of Figure 70 (SEQ ID NO:119), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO943 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 150 or about 201 and about 1661, inclusive, of Figure 69 (SEQ ID NO:118). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203042 (DNA52192-1369) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203042 (DNA52192-1369).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 504, inclusive of Figure 70 (SEQ ID NO:119), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO943 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 504, inclusive of Figure 70 (SEQ ID NO:119), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO943 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 17 in the sequence of Figure 70 (SEQ ID NO:119). The transmembrane domain has been tentatively identified as extending from about amino acid position 376 to about amino acid position 396 in the PRO943 amino acid sequence (Figure 70, SEQ ID NO:119).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 504, inclusive of Figure 70 (SEQ ID NO:119), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO943 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 69 (SEQ ID NO:118).

In another embodiment, the invention provides isolated PRO943 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO943 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 18 to about 504 of Figure 70 (SEQ ID NO:119).

In another aspect, the invention concerns an isolated PRO943 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85 % sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95 % sequence identity to the sequence of amino acid residues 1 or about 18 to about 504, inclusive of Figure 70 (SEQ ID NO:119).

In a further aspect, the invention concerns an isolated PRO943 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 504, inclusive of Figure 70 (SEQ ID NO:119).

In yet another aspect, the invention concerns an isolated PRO943 polypeptide, comprising the sequence of amino acid residues 1 or about 18 to about 504, inclusive of Figure 70 (SEQ ID NO:119), or a fragment thereof sufficient to provide a binding site for an anti-PRO943 antibody. Preferably, the PRO943 fragment retains a qualitative biological activity of a native PRO943 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO943 polypeptide having the sequence of amino acid residues from about 1 or about 18 to about 504, inclusive of Figure 70 (SEQ ID NO:119), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO943 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO943 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO943 polypeptide by contacting the native PRO943 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO943 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

27. **PRO1188**

A cDNA clone (DNA52598-1518) has been identified that encodes a novel polypeptide having homology to nucleotide pyrophosphohydrolase and designated in the present application as "PRO1188."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1188 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1188 polypeptide having the sequence of amino acid residues from about 22 to about 1184, inclusive of Figure 72 (SEQ ID NO:124), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1188 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 199 and about 3687, inclusive, of Figure 71 (SEQ ID NO:123). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203107 (DNA52598-1518), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203107 (DNA52598-1518).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 22 to about 1184, inclusive of Figure 72 (SEQ ID NO:124), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1188 polypeptide having the sequence of amino acid residues from about 22 to about 1184, inclusive of Figure 72 (SEQ ID NO:124), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most

preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1188 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 21 in the sequence of Figure 72 (SEQ ID NO:124).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 22 to about 1184, inclusive of Figure 72 (SEQ ID NO:124), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1188 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1188 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 22 to 1184 of Figure 72 (SEQ ID NO:124).

In another aspect, the invention concerns an isolated PRO1188 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 22 to about 1184, inclusive of Figure 72 (SEQ ID NO:124).

In a further aspect, the invention concerns an isolated PRO1188 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 22 to 1184 of Figure 72 (SEQ ID NO:124).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1188 polypeptide having the sequence of amino acid residues from about 22 to about 1184, inclusive of Figure 72 (SEQ ID NO:124), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1188 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1188 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1188 polypeptide, by contacting the native PRO1188 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1188 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

28. **PRO1133**

A cDNA clone (DNA53913-1490) has been identified that encodes a novel polypeptide having sequence identity with netrin-1a and designated in the present application as "PRO1133."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1133 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1133 polypeptide having the sequence of amino acid residues from about 19 to about 438, inclusive of Figure 74 (SEQ ID NO:129), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1133 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 320 and about 1579, inclusive, of Figure 73 (SEQ ID NO:128). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203162 (DNA53913-1490), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203162 (DNA53913-1490).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 438, inclusive of Figure 74 (SEQ ID NO:129), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1133 polypeptide having the sequence of amino acid residues from about 19 to about 438, inclusive of Figure 74 (SEQ ID NO:129), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to about 438, inclusive of Figure 74 (SEQ ID NO:129), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1133 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1133 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1133 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 19 through 438 of Figure 74 (SEQ ID NO:129).

In another aspect, the invention concerns an isolated PRO1133 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 438, inclusive of Figure 74 (SEQ ID NO:129).

In a further aspect, the invention concerns an isolated PRO1133 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 through 438 of Figure 74 (SEQ ID NO:129).

In yet another aspect, the invention concerns an isolated PRO1133 polypeptide, comprising the sequence of amino acid residues 19 to about 438, inclusive of Figure 74 (SEQ ID NO:129), or a fragment thereof sufficient to provide a binding site for an anti-PRO1133 antibody. Preferably, the PRO1133 fragment retains a qualitative biological activity of a native PRO1133 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1133 polypeptide having the sequence of amino acid residues from about 19 to about 438, inclusive of Figure 74 (SEQ ID NO:129), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1133 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1133 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1133 polypeptide, by contacting the native PRO1133 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1133 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

29. PRO784

A cDNA clone (DNA53978-1443) has been identified that encodes a novel polypeptide, designated in the present application as "PRO784".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO784 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO784 polypeptide having the sequence of amino acid residues from about 16 to about 228, inclusive of Figure 76 (SEQ ID NO:135), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO784 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 182 and about 820, inclusive, of Figure 75 (SEQ ID NO:134). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209983 (DNA53978-1443), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209983 (DNA53978-1443).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 16 to about 228, inclusive of Figure 76 (SEQ ID NO:135), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 50, and preferably at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO784 polypeptide having the sequence of amino acid residues from about 16 to about 228, inclusive of Figure 76 (SEQ ID NO:135), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO784 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position about 1 to about amino acid position 15 in the sequence of Figure 76 (SEQ ID NO: 135). The first transmembrane

domain has been tentatively identified as extending from about amino acid position 68 to about amino acid position 87 in the PRO784 amino acid sequence (Figure 76, SEQ ID NO:135).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to about 228, inclusive of Figure 76 (SEQ ID NO:135), or (b) the complement of the DNA of (a).

In another aspect, the invention concerns hybridization probes that comprise fragments of the PRO784 coding sequence, or complementary sequence thereof. The hybridization probes preferably have at least about 20 nucleotides to about 80 nucleotides, and more preferably, at least about 40 to about 80 nucleotides.

In another embodiment, the invention provides isolated PRO784 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO784 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 16 to 228 of Figure 76 (SEQ ID NO:135).

In another aspect, the invention concerns an isolated PRO784 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 16 to about 228, inclusive of Figure 76 (SEQ ID NO:135).

In a further aspect, the invention concerns an isolated PRO784 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to 228 of Figure 76 (SEQ ID NO:135).

In yet another aspect, the invention concerns an isolated PRO784 polypeptide, comprising the sequence of amino acid residues 16 to about 228, inclusive of Figure 76 (SEQ ID NO: 135), or a fragment thereof sufficient to provide a binding site for an anti-PRO784 antibody. Preferably, the PRO784 fragment retains a qualitative biological activity of a native PRO784 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO784 polypeptide having the sequence of amino acid residues from about 16 to about 228, inclusive of Figure 76 (SEQ ID NO:135), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO784 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO784 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO784 polypeptide, by contacting the native PRO784 polypeptide with a candidate molecule and

monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO784 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

30. **PRO783**

Applicants have identified a cDNA clone that encodes a novel multi-span transmembrane polypeptide, wherein the polypeptide is designated in the present application as "PRO783".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO783 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO783 polypeptide having amino acid residues 1 to 489 of Figure 79 (SEQ ID NO:138), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO783 polypeptide having amino acid residues 1 to X of Figure 79 (SEQ ID NO:138), where X is any amino acid from 19 to 28 of Figure 79 (SEQ ID NO:138), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA53996-1442 vector deposited on June 2, 1998 as ATCC 209921 which includes the nucleotide sequence encoding PRO783.

In another embodiment, the invention provides isolated PRO783 polypeptide. In particular, the invention provides isolated native sequence PRO783 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 489 of Figure 79 (SEQ ID NO:138). Additional embodiments of the present invention are directed to PRO783 polypeptides comprising amino acid 1 to about X of Figure 79 (SEQ ID NO:138), where X is any amino acid from 19 to 28 of Figure 79 (SEQ ID NO:138). Optionally, the PRO783 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA53996-1442 vector deposited on June 2, 1998, as ATCC 209921.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA45201 which comprises the nucleic acid sequence shown in Figure 80 (SEQ ID NO:139).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA14575 which comprises the nucleic acid sequence shown in Figure 81 (SEQ ID NO:140).

31. **PRO820**

A cDNA clone (DNA56041-1416) has been identified, having sequence identity with immunoglobulin gamma Fc receptors that encodes a novel polypeptide, designated in the present application as "PRO820".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO820 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO820 polypeptide having the sequence of amino acid residues from about 1 or 16 to about 124, inclusive of Figure 83 (SEQ ID NO:146),

or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-124, or in another embodiment, 16-124.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO820 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 115 or 160 and about 486, inclusive, of Figure 82 (SEQ ID NO:145). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203021 (DNA56041-1416), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. (DNA56041-1416).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 16 to about 124, inclusive of Figure 83 (SEQ ID NO:146), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO820 polypeptide having the sequence of amino acid residues from about 1 or 16 to about 124, inclusive of Figure 83 (SEQ ID NO:146), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 16 to about 124, inclusive of Figure 83 (SEQ ID NO:146), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO820 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO820 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 16 through 124 of Figure 83 (SEQ ID NO:146).

In another aspect, the invention concerns an isolated PRO820 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more

preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 16 to about 124, inclusive of Figure 83 (SEQ ID NO:146).

In a further aspect, the invention concerns an isolated PRO820 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 16 through 124 of Figure 83 (SEQ ID NO:146).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO820 polypeptide having the sequence of amino acid residues from about 1 or 16 to about 124, inclusive of Figure 83 (SEQ ID NO:146), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO820 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO820 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO820 polypeptide, by contacting the native PRO820 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO820 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

32. **PRO1080**

A cDNA clone (DNA56047-1456) has been identified that encodes a novel polypeptide, designated in the present application as "PRO1080." PRO1080 polypeptides have sequence identity with DnaJ proteins.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1080 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1080 polypeptide having the sequence of amino acid residues from about 1 or 23 to about 358, inclusive of Figure 85 (SEQ ID NO:148), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-358, or in another embodiment, 23-358.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1080 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 159 or 225 and about 1232, inclusive, of Figure 84 (SEQ ID NO:147). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209948 (DNA56047-1456), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209948 (DNA56047-1456).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 23 to about 358, inclusive of Figure 85 (SEQ ID NO:148), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1080 polypeptide having the sequence of amino acid residues from about 1 or 23 to about 358, inclusive of Figure 85 (SEQ ID NO:148), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1080 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 22 in the sequence of Figure 85 (SEQ ID NO:148).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 23 to about 358, inclusive of Figure 85 (SEQ ID NO:148), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1080 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1080 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 23 through 358 of Figure 85 (SEQ ID NO:148).

In another aspect, the invention concerns an isolated PRO1080 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 23 to about 358, inclusive of Figure 85 (SEQ ID NO:148).

In a further aspect, the invention concerns an isolated PRO1080 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 23 through 358 of Figure 85 (SEQ ID NO:148).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1080 polypeptide having the sequence of amino acid residues from about 1 or 23 to about 358, inclusive of Figure 85 (SEQ ID NO:148), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1080 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1080 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1080 polypeptide, by contacting the native PRO1080 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1080 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA36527 comprising the nucleotide sequence of Figure 86 (SEQ ID NO:149).

33. **PRO1079**

A cDNA clone (DNA56050-1455) has been identified that encodes a novel polypeptide, designated in the present application as "PRO1079".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1079 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1079 polypeptide having the sequence of amino acid residues from about 30 to about 226, inclusive of Figure 88 (SEQ ID NO:151), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1079 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 270 and about 860, inclusive, of Figure 87 (SEQ ID NO:150). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least

about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203011 (DNA56050-1455), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203011 (DNA56050-1455).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 30 to about 226, inclusive of Figure 88 (SEQ ID NO:151), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides and preferably at least about 100 nucleotides, and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1079 polypeptide having the sequence of amino acid residues from about 30 to about 226, inclusive of Figure 88 (SEQ ID NO:151), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1079 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 29 in the sequence of Figure 88 (SEQ ID NO:151).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 30 to about 226, inclusive of Figure 88 (SEQ ID NO:151), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1079 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1079 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1079 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 30 to 226 of Figure 88 (SEQ ID NO:151).

In another aspect, the invention concerns an isolated PRO1079 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 30 to about 226, inclusive of Figure 88 (SEQ ID NO:151).

In a further aspect, the invention concerns an isolated PRO1079 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 30 to 226 of Figure 88 (SEQ ID NO:151).

In yet another aspect, the invention concerns an isolated PRO1079 polypeptide, comprising the sequence of amino acid residues 30 to about 226, inclusive of Figure 88 (SEQ ID NO:151), or a fragment thereof sufficient to provide a binding site for an anti-PRO1079 antibody. Preferably, the PRO1079 fragment retains a qualitative biological activity of a native PRO1079 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1079 polypeptide having the sequence of amino acid residues from about 30 to about 226, inclusive of Figure 88 (SEQ ID NO:151), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

34. **PRO793**

A cDNA clone (DNA56110-1437) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO793".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO793 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO793 polypeptide having the sequence of amino acid residues from about 1 to about 138, inclusive of Figure 90 (SEQ ID NO:153), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO793 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 77 and about 490, inclusive, of Figure 89 (SEQ ID NO:152). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203113 (DNA56110-1437) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203113 (DNA56110-1437).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 138, inclusive of Figure 90 (SEQ ID NO:153), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO793 polypeptide having the sequence of amino acid residues from 1 to about 138, inclusive of Figure 90 (SEQ ID NO:153), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO793 polypeptide, with or without the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains have been tentatively identified as extending from about amino acid position 12 to about amino acid position 30, from about amino acid position 33 to about amino acid position 52, from about amino acid position 69 to about amino acid position 89 and from about amino acid position 93 to about amino acid position 109 in the PRO793 amino acid sequence (Figure 90, SEQ ID NO:153).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 138, inclusive of Figure 90 (SEQ ID NO:153), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO793 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 89 (SEQ ID NO:152).

In another embodiment, the invention provides isolated PRO793 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO793 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 138 of Figure 90 (SEQ ID NO:153).

In another aspect, the invention concerns an isolated PRO793 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 138, inclusive of Figure 90 (SEQ ID NO:153).

In a further aspect, the invention concerns an isolated PRO793 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 138, inclusive of Figure 90 (SEQ ID NO:153).

In yet another aspect, the invention concerns an isolated PRO793 polypeptide, comprising the sequence of amino acid residues 1 to about 138, inclusive of Figure 90 (SEQ ID NO:153), or a fragment thereof sufficient to provide a binding site for an anti-PRO793 antibody. Preferably, the PRO793 fragment retains a qualitative biological activity of a native PRO793 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO793 polypeptide having the sequence of amino acid residues from about 1 to about 138, inclusive of Figure 90 (SEQ ID NO:153), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA50177 comprising the nucleotide sequence of Figure 91 (SEQ ID NO:154).

35. **PRO1016**

A cDNA clone (DNA56113-1378) has been identified, having sequence identity with acyltransferases that encodes a novel polypeptide, designated in the present application as "PRO1016".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1016 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1016 polypeptide having the sequence of amino acid residues from about 1 or 19 to about 378, inclusive of Figure 93 (SEQ ID NO:156), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-378, or in another embodiment, 19-378.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1016 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 168 or 222 and about 1301, inclusive, of Figure 92 (SEQ ID NO:155). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule

encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203049 (DNA56113-1378), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203049 (DNA56113-1378).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 19 to about 378, inclusive of Figure 93 (SEQ ID NO:156), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1016 polypeptide having the sequence of amino acid residues from about 1 or 19 to about 378, inclusive of Figure 93 (SEQ ID NO:156), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1016 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 18 in the sequence of Figure 93 (SEQ ID NO:156). The transmembrane domains have been tentatively identified as extending from about amino acid position 305 through about amino acid position 330 and from about amino acid position 332 through about amino acid position 352 in the PRO1016 amino acid sequence (Figure 93, SEQ ID NO:156).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 19 to about 378, inclusive of Figure 93 (SEQ ID NO:156), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1016 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1016 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 19 through 378 of Figure 93 (SEQ ID NO:156).

In another aspect, the invention concerns an isolated PRO1016 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 19 to about 378, inclusive of Figure 93 (SEQ ID NO:156).

In a further aspect, the invention concerns an isolated PRO1016 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 19 through 378 of Figure 93 (SEQ ID NO:156).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1016 polypeptide having the sequence of amino acid residues from about 1 or 19 to about 378, inclusive of Figure 93 (SEQ ID NO:156), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1016 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1016 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1016 polypeptide, by contacting the native PRO1016 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1016 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

36. **PRO1013**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with P120, wherein the polypeptide is designated in the present application as "PRO1013".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1013 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1013 polypeptide having amino acid residues 1 through 409 of Figure 95 (SEQ ID NO: 158), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on June 2, 1998 with the ATCC as DNA56410-1414 which includes the nucleotide sequence encoding PRO1013.

In another embodiment, the invention provides isolated PRO1013 polypeptide. In particular, the invention provides isolated native sequence PRO1013 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 409 of Figure 95 (SEQ ID NO:158). Optionally, the PRO1013 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on June 2, 1998 with the ATCC as DNA56410-1414.

37. PRO937

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to glypican family proteins, wherein the polypeptide is designated in the present application as "PRO937".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO937 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO937 polypeptide having amino acid residues 1 to 556 of Figure 97 (SEQ ID NO:160), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO937 polypeptide having amino acid residues about 23 to 556 of Figure 97 (SEQ ID NO:160), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA56436-1448 vector deposited on May 27, 1998, as ATCC 209902 which includes the nucleotide sequence encoding PRO937.

In another embodiment, the invention provides isolated PRO937 polypeptide. In particular, the invention provides isolated native sequence PRO937 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 556 of Figure 97 (SEQ ID NO:160). Additional embodiments of the present invention are directed to PRO937 polypeptides comprising amino acids about 23 to 556 of Figure 97 (SEQ ID NO:160). Optionally, the PRO937 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA56436-1448 vector deposited on May 27, 1998 as ATCC 209902.

38. PRO842

A cDNA clone (DNA56855-1447) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO842."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO842 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO842 polypeptide having the sequence of amino acid residues from about 23 to about 119, inclusive of Figure 99 (SEQ ID NO:165), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO842 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 219 and about 509, inclusive, of Figure 98 (SEQ ID NO:164). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule

encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203004 (DNA56855-1447), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203004 (DNA56855-1447).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 23 to about 119, inclusive of Figure 99 (SEQ ID NO:165), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides, and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO842 polypeptide having the sequence of amino acid residues from about 23 to about 119, inclusive of Figure 99 (SEQ ID NO:165), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO842 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 22 in the sequence of Figure 99 (SEQ ID NO:165).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 23 to about 119, inclusive of Figure 99 (SEQ ID NO:165), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO842 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO842 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO842 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 23 to 119 of Figure 99 (SEQ ID NO:165).

In another aspect, the invention concerns an isolated PRO842 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 23 to about 119, inclusive of Figure 99 (SEQ ID NO:165).

In a further aspect, the invention concerns an isolated PRO842 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 23 to 119 of Figure 99 (SEQ ID NO:165).

In yet another aspect, the invention concerns an isolated PRO842 polypeptide, comprising the sequence of amino acid residues 23 to about 119, inclusive of Figure 99 (SEQ ID NO:165), or a fragment thereof sufficient to provide a binding site for an anti-PRO842 antibody. Preferably, the PRO842 fragment retains a qualitative biological activity of a native PRO842 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO842 polypeptide having the sequence of amino acid residues from about 23 to about 119, inclusive of Figure 99 (SEQ ID NO:165), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

39. **PRO839**

A cDNA clone (DNA56859-1445) has been identified that encodes a novel polypeptide, designated in the present application as "PRO839."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO839 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO839 polypeptide having the sequence of amino acid residues from about 24 to about 87, inclusive of Figure 101 (SEQ ID NO:167), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO839 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 71 and about 262, inclusive, of Figure 100 (SEQ ID NO:166). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203019 (DNA56859-1445), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203019 (DNA56859-1445).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 24 to about 87, inclusive of Figure 101 (SEQ ID NO:167), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 50 nucleotides, and preferably at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO839 polypeptide having the sequence of amino acid residues from about 24 to about 87, inclusive of Figure 101 (SEQ ID NO: 167), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO839 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 23 in the sequence of Figure 101 (SEQ ID NO:167).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 24 to about 87, inclusive of Figure 101 (SEQ ID NO:167), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO839 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO839 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO839 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 24 to 87 of Figure 101 (SEQ ID NO:167).

In another aspect, the invention concerns an isolated PRO839 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 24 to about 87, inclusive of Figure 101 (SEQ ID NO:167).

In a further aspect, the invention concerns an isolated PRO839 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 24 to 87 of Figure 101 (SEQ ID NO:167).

In yet another aspect, the invention concerns an isolated PRO839 polypeptide, comprising the sequence of amino acid residues 24 to about 87, inclusive of Figure 101 (SEQ ID NO:167), or a fragment thereof sufficient to provide a binding site for an anti-PRO839 antibody. Preferably, the PRO839 fragment retains a qualitative biological activity of a native PRO839 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO839 polypeptide having the sequence of amino acid residues from about 24 to about 87, inclusive of Figure 101 (SEQ ID NO:167), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

40. **PRO1180**

Applicants have identified a cDNA clone (DNA56860-1510) having homology to nucleic acid encoding methyltransferase enzymes that encodes a novel polypeptide, designated in the present application as "PRO1180".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1180 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1180 polypeptide having the sequence of amino acid residues from about 1 or about 24 to about 277, inclusive of Figure 103 (SEQ ID NO:169), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1180 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 78 or about 147 and about 908, inclusive of Figure 102 (SEQ ID NO:168). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209952 (DNA56860-1510). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209952 (DNA56860-1510).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 24 to about 277, inclusive of Figure 103 (SEQ ID

NO:169).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1180 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 23 in the sequence of Figure 103 (SEQ ID NO:169).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 24 to about 277, inclusive of Figure 103 (SEQ ID NO:169).

Another embodiment is directed to fragments of a PRO1180 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1180 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1180 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 24 to about 277 of Figure 103 (SEQ ID NO:169).

In another aspect, the invention concerns an isolated PRO1180 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 24 to about 277, inclusive of Figure 103 (SEQ ID NO:169).

In a further aspect, the invention concerns an isolated PRO1180 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 24 to about 277, inclusive of Figure 103 (SEQ ID NO:169).

In yet another aspect, the invention concerns an isolated PRO1180 polypeptide, comprising the sequence of amino acid residues 1 or about 24 to about 277, inclusive of Figure 103 (SEQ ID NO:169), or a fragment thereof sufficient to provide a binding site for an anti-PRO1180 antibody. Preferably, the PRO1180 fragment retains a qualitative biological activity of a native PRO1180 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1180 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1180 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1180 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of a native PRO1180 polypeptide.

In still a further embodiment, the invention concerns a composition comprising a PRO1180 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

41. **PRO1134**

A cDNA clone (DNA56865-1491) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO1134".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1134 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1134 polypeptide having the sequence of amino acid residues from about 1 or about 24 to about 371, inclusive of Figure 105 (SEQ ID NO:171), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1134 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 153 or about 222 and about 1265, inclusive, of Figure 104 (SEQ ID NO:170). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203022 (DNA56865-1491) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203022 (DNA56865-1491).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 24 to about 371, inclusive of Figure 105 (SEQ ID NO:171), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1134 polypeptide having the sequence of amino acid residues from 1 or about 24 to about 371, inclusive of Figure 105 (SEQ ID NO:171), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1134 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is

complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 23 in the sequence of Figure 105 (SEQ ID NO:171).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 24 to about 371, inclusive of Figure 105 (SEQ ID NO:171), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1134 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 104 (SEQ ID NO:170).

In another embodiment, the invention provides isolated PRO1134 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1134 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 24 to about 371 of Figure 105 (SEQ ID NO:171).

In another aspect, the invention concerns an isolated PRO1134 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 24 to about 371, inclusive of Figure 105 (SEQ ID NO:171).

In a further aspect, the invention concerns an isolated PRO1134 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 24 to about 371, inclusive of Figure 105 (SEQ ID NO:171).

In yet another aspect, the invention concerns an isolated PRO1134 polypeptide, comprising the sequence of amino acid residues 1 or about 24 to about 371, inclusive of Figure 105 (SEQ ID NO:171), or a fragment thereof sufficient to provide a binding site for an anti-PRO1134 antibody. Preferably, the PRO1134 fragment retains a qualitative biological activity of a native PRO1134 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1134 polypeptide having the sequence of amino acid residues from about 1 or about 24 to about 371, inclusive of Figure 105 (SEQ ID NO:171), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA52352 comprising the nucleotide sequence of SEQ ID NO:172 (see Figure 106).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA55725 comprising the nucleotide sequence of SEQ ID NO:173 (see Figure 107).

42. **PRO830**

A cDNA clone (DNA56866-1342) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO830".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO830 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO830 polypeptide having the sequence of amino acid residues from about 1 or about 34 to about 87, inclusive of Figure 109 (SEQ ID NO:175), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO830 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 154 or about 253 and about 414, inclusive, of Figure 108 (SEQ ID NO:174). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203023 (DNA56866-1342) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203023 (DNA56866-1342).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 34 to about 87, inclusive of Figure 109 (SEQ ID NO:175), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO830 polypeptide having the sequence of amino acid residues from 1 or about 34 to about 87, inclusive of Figure 109 (SEQ ID NO:175), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO830 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 33 in the sequence of Figure 109 (SEQ ID NO:175).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 34 to about 87, inclusive of Figure 109 (SEQ ID NO:175), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO830 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 108 (SEQ ID NO:174).

In another embodiment, the invention provides isolated PRO830 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO830 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 34 to about 87 of Figure 109 (SEQ ID NO:175).

In another aspect, the invention concerns an isolated PRO830 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 34 to about 87, inclusive of Figure 109 (SEQ ID NO:175).

In a further aspect, the invention concerns an isolated PRO830 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 34 to about 87, inclusive of Figure 109 (SEQ ID NO:175).

In yet another aspect, the invention concerns an isolated PRO830 polypeptide, comprising the sequence of amino acid residues 1 or about 34 to about 87, inclusive of Figure 109 (SEQ ID NO:175), or a fragment thereof sufficient to provide a binding site for an anti-PRO830 antibody. Preferably, the PRO830 fragment retains a qualitative biological activity of a native PRO830 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO830 polypeptide having the sequence of amino acid residues from about 1 or about 34 to about 87, inclusive of Figure 109 (SEQ ID NO:175), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host

cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

43. PRO1115

A cDNA clone (DNA56868-1478) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1115".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1115 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1115 polypeptide having the sequence of amino acid residues from about 21 to about 445, inclusive of Figure 111 (SEQ ID NO:177), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1115 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 249 and about 1523, inclusive, of Figure 110 (SEQ ID NO:176). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203024 (DNA56868-1478), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203024 (DNA56868-1478).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 21 to about 445, inclusive of Figure 111 (SEQ ID NO:177), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1115 polypeptide having the sequence of amino acid residues from about 21 to about 445, inclusive of Figure 111 (SEQ ID NO: 177), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1115 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and

one or more of its transmembrane domains deleted or inactivated, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 111 (SEQ ID NO: 177). Transmembrane domains have been tentatively identified as extending from about amino acid positions 35-54, 75-97, 126-146, 185-204, 333-350, and 352-371 in the PRO1115 amino acid sequence (Figure 111, SEQ ID NO: 177).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to about 445, inclusive of Figure 111 (SEQ ID NO:177), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1115 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1115 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1115 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 21 to 445 of Figure 111 (SEQ ID NO:177).

In another aspect, the invention concerns an isolated PRO1115 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 21 to about 445, inclusive of Figure 111 (SEQ ID NO:177).

In a further aspect, the invention concerns an isolated PRO1115 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to 445 of Figure 111 (SEQ ID NO:177).

In yet another aspect, the invention concerns an isolated PRO1115 polypeptide, comprising the sequence of amino acid residues 21 to about 445, inclusive of Figure 111 (SEQ ID NO:177), or a fragment thereof sufficient to provide a binding site for an anti-PRO1115 antibody. Preferably, the PRO1115 fragment retains a qualitative biological activity of a native PRO1115 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1115 polypeptide having the sequence of amino acid residues from about 21 to about 445, inclusive of Figure 111 (SEQ ID NO:177), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

44. **PRO1277**

A cDNA clone (DNA56869-1545) has been identified that encodes a novel polypeptide having homology to Coch-5B2 and designated in the present application as "PRO1277."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1277 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1277 polypeptide having the sequence of amino acid residues from about 27 to about 678, inclusive of Figure 113 (SEQ ID NO:179), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1277 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 266 and about 2221, inclusive, of Figure 112 (SEQ ID NO:178). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203161 (DNA56869-1545), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203161 (DNA56869-1545).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 27 to about 678, inclusive of Figure 113 (SEQ ID NO:179), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1277 polypeptide having the sequence of amino acid residues from about 27 to about 678, inclusive of Figure 113 (SEQ ID NO:179), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1277 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 26 in the sequence of Figure 113 (SEQ ID NO:179). The transmembrane

domain has been tentatively identified as extending from about amino acid position 181 to about amino acid position 200 in the PRO1277 amino acid sequence (Figure 113, SEQ ID NO:179).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 27 to about 678, inclusive of Figure 113 (SEQ ID NO:179), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1277 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1277 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1277 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 27 to 678 of Figure 113 (SEQ ID NO:179).

In another aspect, the invention concerns an isolated PRO1277 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 27 to about 678, inclusive of Figure 113 (SEQ ID NO:179).

In a further aspect, the invention concerns an isolated PRO1277 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 27 to 678 of Figure 113 (SEQ ID NO:179).

In yet another aspect, the invention concerns an isolated PRO1277 polypeptide, comprising the sequence of amino acid residues 27 to about 678, inclusive of Figure 113 (SEQ ID NO:179), or a fragment thereof sufficient to provide a binding site for an anti-PRO1277 antibody. Preferably, the PRO1277 fragment retains a qualitative biological activity of a native PRO1277 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1277 polypeptide having the sequence of amino acid residues from about 27 to about 678, inclusive of Figure 113 (SEQ ID NO:179), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1277 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1277 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1277 polypeptide, by contacting the native PRO1277 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1277 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

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45. **PRO1135**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to alpha 1,2-mannosidase, wherein the polypeptide is designated in the present application as "PRO1135".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding
10 a PRO1135 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1135 polypeptide having amino acid residues 1 to 541 of Figure 115 (SEQ ID NO:181), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO1135 polypeptide having amino acid residues about 22 to 541 of Figure 115 (SEQ ID NO:181), or is complementary
15 to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA56870-1492 vector deposited on June 2, 1998 as ATCC 209925 which includes the nucleotide sequence encoding PRO1135.

In another embodiment, the invention provides isolated PRO1135 polypeptide. In particular, the
20 invention provides isolated native sequence PRO1135 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 541 of Figure 115 (SEQ ID NO:181). Additional embodiments of the present invention are directed to PRO1135 polypeptides comprising amino acids about 22 to 541 of Figure 115 (SEQ ID NO:181). Optionally, the PRO1135 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA56870-1492 vector deposited on June 2, 1998 as ATCC
25 209925.

46. **PRO1114**

A cDNA clone (DNA57033-1403) has been identified that encodes a novel interferon receptor polypeptide, designated in the present application as "PRO1114 interferon receptor".

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1114 interferon receptor polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1114 interferon receptor
35 polypeptide having the sequence of amino acid residues from about 1 or about 30 to about 311, inclusive of Figure 117 (SEQ ID NO:183), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1114 interferon receptor polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 250 or about 337 and about 1182, inclusive, of Figure 116 (SEQ ID NO:182). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209905 (DNA57033-1403) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209905 (DNA57033-1403).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 30 to about 311, inclusive of Figure 117 (SEQ ID NO:183), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1114 interferon receptor polypeptide having the sequence of amino acid residues from 1 or about 30 to about 311, inclusive of Figure 117 (SEQ ID NO:183), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1114 interferon receptor polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 29 in the sequence of Figure 117 (SEQ ID NO:183). The transmembrane domain has been tentatively identified as extending from about amino acid position 230 to about amino acid position 255 in the PRO1114 interferon receptor amino acid sequence (Figure 117, SEQ ID NO:183).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 30 to about 311, inclusive of Figure 117 (SEQ ID NO:183), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1114 interferon receptor polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80

nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 116 (SEQ ID NO:182).

In another embodiment, the invention provides isolated PRO1114 interferon receptor polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1114 interferon receptor polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 30 to about 311 of Figure 117 (SEQ ID NO:183).

In another aspect, the invention concerns an isolated PRO1114 interferon receptor polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 30 to about 311, inclusive of Figure 117 (SEQ ID NO:183).

In a further aspect, the invention concerns an isolated PRO1114 interferon receptor polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 30 to about 311, inclusive of Figure 117 (SEQ ID NO:183).

In yet another aspect, the invention concerns an isolated PRO1114 interferon receptor polypeptide, comprising the sequence of amino acid residues 1 or about 30 to about 311, inclusive of Figure 117 (SEQ ID NO:183), or a fragment thereof sufficient to provide a binding site for an anti-PRO1114 interferon receptor antibody. Preferably, the PRO1114 interferon receptor fragment retains a qualitative biological activity of a native PRO1114 interferon receptor polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1114 interferon receptor polypeptide having the sequence of amino acid residues from about 1 or about 30 to about 311, inclusive of Figure 117 (SEQ ID NO:183), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1114 interferon receptor polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1114 interferon receptor antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1114 interferon receptor polypeptide by contacting the native PRO1114 interferon receptor polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1114 interferon receptor polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically

acceptable carrier.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA48466 comprising the nucleotide sequence of SEQ ID NO:184 (see Figure 118).

47. **PRO828**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to glutathione peroxidases wherein the polypeptide is designated in the present application as "PRO828".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO828 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO828 polypeptide having amino acid residues 1 to 187 of Figure 120 (SEQ ID NO:189), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO828 polypeptide having amino acid residues about 22 to 187 of Figure 120 (SEQ ID NO:189), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA57037-1444 vector deposited on May 27, 1998 as ATCC 209903 which includes the nucleotide sequence encoding PRO828.

In another embodiment, the invention provides isolated PRO828 polypeptide. In particular, the invention provides isolated native sequence PRO828 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 187 of Figure 120 (SEQ ID NO:189). Additional embodiments of the present invention are directed to PRO828 polypeptides comprising amino acids about 22 to 187 of Figure 120 (SEQ ID NO:189). Optionally, the PRO828 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA57037-1444 vector deposited on May 27, 1998 as ATCC 209903.

48. **PRO1009**

A cDNA clone (DNA57129-1413) has been identified, having sequence identity with a long chain acyl-CoA synthetase homologue, a long chain acyl-CoA synthetase and a long chain acyl-CoA synthetase ligase that encodes a novel polypeptide, designated in the present application as "PRO1009."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1009 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1009 polypeptide having the sequence of amino acid residues from about 1 or 23 to about 615, inclusive of Figure 122 (SEQ ID NO:194), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two separate alternative embodiments provided herein, i.e., 1-615 or 23-615.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1009 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 41 or 107 and about 1885, inclusive, of Figure 121 (SEQ ID NO:193). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209977 (DNA57129-1413), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209977 (DNA57129-1413).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 23 to about 615, inclusive of Figure 122 (SEQ ID NO:194), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1009 polypeptide having the sequence of amino acid residues from about 1 or 23 to about 615, inclusive of Figure 122 (SEQ ID NO:194), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1009 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 to about amino acid position 22 in the sequence of Figure 122 (SEQ ID NO:194). The transmembrane domains have been tentatively identified as extending from about amino acid positions 140-161, 213-229 and 312-334 in the PRO1009 amino acid sequence (Figure 122, SEQ ID NO:194).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 23 to about 615, inclusive of Figure 122 (SEQ ID NO:194), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1009 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1009 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 23 to 615 of Figure 122 (SEQ ID NO:194).

In another aspect, the invention concerns an isolated PRO1009 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 23 to about 615, inclusive of Figure 122 (SEQ ID NO:194).

In a further aspect, the invention concerns an isolated PRO1009 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 23 to 615 of Figure 122 (SEQ ID NO:194).

In yet another aspect, the invention concerns an isolated PRO1009 polypeptide, comprising the sequence of amino acid residues 1 or 23 to about 615, inclusive of Figure 122 (SEQ ID NO:194), or a fragment thereof sufficient to provide a binding site for an anti-PRO1009 antibody. Preferably, the PRO1009 fragment retains a qualitative biological activity of a native PRO1009 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1009 polypeptide having the sequence of amino acid residues from about 1 or 23 through about 615, inclusive of Figure 122 (SEQ ID NO:194), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1009 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1009 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1009 polypeptide, by contacting the native PRO1009 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1009 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA50853 comprising the nucleotide sequence of Figure 123 (SEQ ID NO:195).

49. PRO1007

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with MAGPIAP, wherein the polypeptide is designated in the present application as "PRO1007".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1007 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1007

polypeptide having amino acid residues 1 through 346 of Figure 125 (SEQ ID NO:197), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on June 9, 1998 with the ATCC as DNA57690-1374 which includes the nucleotide sequence encoding PRO1007.

In another embodiment, the invention provides isolated PRO1007 polypeptide. In particular, the invention provides isolated native sequence PRO1007 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 346 of Figure 125 (SEQ ID NO:197). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO1007 polypeptide. Optionally, the PRO1007 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited with the ATCC on June 9, 1998 as DNA57690-1374.

50. **PRO1056**

A cDNA clone (DNA57693-1424) has been identified, having homology to nucleic acid encoding a chloride channel protein that encodes a novel polypeptide, designated in the present application as "PRO1056".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1056 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1056 polypeptide having the sequence of amino acid residues from about 1 or about 19 to about 120, inclusive of Figure 127 (SEQ ID NO:199), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1056 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 56 or about 110 and about 415, inclusive, of Figure 126 (SEQ ID NO:198). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203008 (DNA57693-1424) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203008 (DNA57693-1424).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 19 to about 120, inclusive of Figure 127 (SEQ ID NO:199), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1056 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 120, inclusive of Figure 127 (SEQ ID NO:199), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1056 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 18 in the sequence of Figure 127 (SEQ ID NO:199). The transmembrane domain has been tentatively identified as extending from about amino acid position 39 to about amino acid position 58 in the PRO1056 amino acid sequence (Figure 127, SEQ ID NO:199).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 19 to about 120, inclusive of Figure 127 (SEQ ID NO:199), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1056 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 126 (SEQ ID NO:198).

In another embodiment, the invention provides isolated PRO1056 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1056 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 19 to about 120 of Figure 127 (SEQ ID NO:199).

In another aspect, the invention concerns an isolated PRO1056 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 19 to about 120, inclusive of Figure 127 (SEQ ID NO:199).

In a further aspect, the invention concerns an isolated PRO1056 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 19 to about 120, inclusive of Figure 127 (SEQ ID NO:199).

In yet another aspect, the invention concerns an isolated PRO1056 polypeptide, comprising the sequence of amino acid residues 1 or about 19 to about 120, inclusive of Figure 127 (SEQ ID NO:199), or a fragment thereof sufficient to provide a binding site for an anti-PRO1056 antibody. Preferably, the PRO1056 fragment retains a qualitative biological activity of a native PRO1056 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1056 polypeptide having the sequence of amino acid residues from about 1 or about 19 to about 120, inclusive of Figure 127 (SEQ ID NO:199), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1056 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1056 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1056 polypeptide by contacting the native PRO1056 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1056 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

51. **PRO826**

A cDNA clone (DNA57694-1341) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO826".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO826 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO826 polypeptide having the sequence of amino acid residues from about 1 or about 23 to about 99, inclusive of Figure 129 (SEQ ID NO:201), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO826 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 13 or about 79 and about 309, inclusive, of Figure 128 (SEQ ID NO:200). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203017

(DNA57694-1341) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203017 (DNA57694-1341).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 23 to about 99, inclusive of Figure 129 (SEQ ID NO:201), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO826 polypeptide having the sequence of amino acid residues from 1 or about 23 to about 99, inclusive of Figure 129 (SEQ ID NO:201), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO826 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 22 in the sequence of Figure 129 (SEQ ID NO:201).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 23 to about 99, inclusive of Figure 129 (SEQ ID NO:201), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO826 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 128 (SEQ ID NO:200).

In another embodiment, the invention provides isolated PRO826 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO826 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 23 to about 99 of Figure 129 (SEQ ID NO:201).

In another aspect, the invention concerns an isolated PRO826 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the

sequence of amino acid residues 1 or about 23 to about 99, inclusive of Figure 129 (SEQ ID NO:201).

In a further aspect, the invention concerns an isolated PRO826 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 23 to about 99, inclusive of Figure 129 (SEQ ID NO:201).

In yet another aspect, the invention concerns an isolated PRO826 polypeptide, comprising the sequence of amino acid residues 1 or about 23 to about 99, inclusive of Figure 129 (SEQ ID NO:201), or a fragment thereof sufficient to provide a binding site for an anti-PRO826 antibody. Preferably, the PRO826 fragment retains a qualitative biological activity of a native PRO826 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO826 polypeptide having the sequence of amino acid residues from about 1 or about 23 to about 99, inclusive of Figure 129 (SEQ ID NO:201), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

52. **PRO819**

A cDNA clone (DNA57695-1340) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO819".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO819 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO819 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 52, inclusive of Figure 131 (SEQ ID NO:203), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO819 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 46 or about 118 and about 201, inclusive, of Figure 130 (SEQ ID NO:202). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203006 (DNA57695-1340) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in

ATCC Deposit No. 203006 (DNA57695-1340).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 52, inclusive of Figure 131 (SEQ ID NO:203), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO819 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 52, inclusive of Figure 131 (SEQ ID NO:203), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO819 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 24 in the sequence of Figure 131 (SEQ ID NO:203).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 52, inclusive of Figure 131 (SEQ ID NO:203), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO819 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 130 (SEQ ID NO:202).

In another embodiment, the invention provides isolated PRO819 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO819 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 25 to about 52 of Figure 131 (SEQ ID NO:203).

In another aspect, the invention concerns an isolated PRO819 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 52, inclusive of Figure 131 (SEQ ID NO:203).

In a further aspect, the invention concerns an isolated PRO819 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 52, inclusive of Figure 131 (SEQ ID NO:203).

In yet another aspect, the invention concerns an isolated PRO819 polypeptide, comprising the sequence of amino acid residues 1 or about 25 to about 52, inclusive of Figure 131 (SEQ ID NO:203), or a fragment thereof sufficient to provide a binding site for an anti-PRO819 antibody. Preferably, the PRO819 fragment retains a qualitative biological activity of a native PRO819 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO819 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 52, inclusive of Figure 131 (SEQ ID NO:203), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

53. **PRO1006**

A cDNA clone (DNA57699-1412) has been identified, having sequence identity with a virud protein believed to be a tyrosine protein kinase, that encodes a novel polypeptide, designated in the present application as "PRO1006."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1006 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1006 polypeptide having the sequence of amino acid residues from about 1 or 24 to about 392, inclusive of Figure 133 (SEQ ID NO:205), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-392, or in another embodiment, 24-392.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1006 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 28 or 97 and about 1203, inclusive, of Figure 132 (SEQ ID NO:204). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203020

(DNA57699-1412), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203020 (DNA57699-1412).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 24 to about 392, inclusive of Figure 133 (SEQ ID NO:205), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1006 polypeptide having the sequence of amino acid residues from about 1 or 24 to about 392, inclusive of Figure 133 (SEQ ID NO:205), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 24 to about 392, inclusive of Figure 133 (SEQ ID NO:205), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1006 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1006 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 24 through 392 of Figure 133 (SEQ ID NO:205).

In another aspect, the invention concerns an isolated PRO1006 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 24 to about 392, inclusive of Figure 133 (SEQ ID NO:205).

In a further aspect, the invention concerns an isolated PRO1006 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 24 through 392 of Figure 133 (SEQ ID NO:205).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1006 polypeptide having the sequence of amino acid residues from about 1 or 24 to about 392, inclusive of Figure 133 (SEQ ID NO:205), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90%

sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1006 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1006 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1006 polypeptide, by contacting the native PRO1006 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1006 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

54. **PRO1112**

Applicants have identified a cDNA clone that encodes a novel polypeptide having multiple transmembrane domains and having some sequence identity with a Mycobacterium tuberculosis peptide, a peptide found in a Dayhoff database designated as "MTY20B11_13", wherein the novel polypeptide is designated in the present application as "PRO1112".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1112 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1112 polypeptide having the sequence of amino acid residues from 1 or about 14 through about 262 of Figure 135 (SEQ ID NO:207), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1112 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues about 20 or 59 through 809 of Figure 134 (SEQ ID NO:206). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in the ATCC Deposit of DNA57702-1476 made on June 9, 1998. In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in the ATCC Deposit of DNA57702-1476 made on June 9, 1998.

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 14 through about 262 of Figure 135 (SEQ ID

NO:207).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1112 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 13 of Figure 135 (SEQ ID NO:207). The transmembrane domains have been tentatively identified as extending from about amino acid positions 58-76, 99-113, 141-159 and 203-222 of Figure 135 (SEQ ID NO:207).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 14 through 262 of Figure 135 (SEQ ID NO:207).

Another embodiment is directed to fragments of a PRO1112 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 60 to about 100 nucleotides in length.

In another embodiment, the invention provides isolated PRO1112 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1112 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 14 through about 262 of Figure 135 (SEQ ID NO:207).

In another aspect, the invention concerns an isolated PRO1112 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 14 through about 262 of Figure 135 (SEQ ID NO:207).

In a further aspect, the invention concerns an isolated PRO1112 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 14 through about 262 of Figure 135 (SEQ ID NO:207).

In yet another aspect, the invention concerns an isolated PRO1112 polypeptide, comprising the sequence of amino acid residues 1 or about 14 through about 262 of Figure 135 (SEQ ID NO:207), or a fragment thereof sufficient to provide a binding site for an anti-PRO1112 antibody. Preferably, the PRO1112 fragment retains a qualitative biological activity of a native PRO1112 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1112 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

55. **PRO1074**

Applicants have identified a cDNA clone, DNA57704-1452, that encodes a novel polypeptide having homology to galactosyltransferase, wherein the polypeptide is designated in the present application as "PRO1074".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1074 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1074 polypeptide having the sequence of amino acid residues from 1 to about 331, inclusive of Figure 137 (SEQ ID NO:209), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1074 polypeptide comprising DNA that hybridizes to the complement of the nucleic acid sequence having about residues 322 to 1314, inclusive of Figure 136 (SEQ ID NO:208). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209953 (DNA57704-1452), which was deposited on June 9, 1998, or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209953 (DNA57704-1452).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 331, inclusive of Figure 137 (SEQ ID NO:209).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1074 extracellular domain (ECD), with or without the initiating methionine, and its soluble variants (i.e. transmembrane domain(s) deleted or inactivated) or is complementary to such encoding nucleic acid molecule. A type II transmembrane domain region has been tentatively identified as extending from about amino acid position 20 to 39 in the PRO1074 amino acid sequence (Figure 137, SEQ ID NO:209).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 90% positives, and most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 331, inclusive of Figure 137 (SEQ ID NO:209).

Another embodiment is directed to fragments of a PRO1074 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1074 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1074 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 331 of Figure 137 (SEQ ID NO:209).

In another aspect, the invention concerns an isolated PRO1074 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to 331, inclusive of Figure 137 (SEQ ID NO:209).

In a further aspect, the invention concerns an isolated PRO1074 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, and most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 331 of Figure 137 (SEQ ID NO:209).

In another aspect, the invention concerns a PRO1074 extracellular domain comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to the sequence of amino acid residues X to 331 of Figure 2 (SEQ ID NO:3), wherein X is any one of amino acid residues 35 to 44 of Figure 137 (SEQ ID NO:209).

In yet another aspect, the invention concerns an isolated PRO1074 polypeptide, comprising the sequence of amino acid residues 1 to about 331, inclusive of Figure 137 (SEQ ID NO:209), or a fragment thereof sufficient to provide a binding site for an anti-PRO1074 antibody. Preferably, the PRO1074 fragment retains a qualitative biological activity of a native PRO1074 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1074 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

In yet another embodiment, the invention concerns agonist and antagonists of the PRO1074 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1074 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of a native PRO1074 polypeptide.

In still a further embodiment, the invention concerns a composition comprising a PRO1074 polypeptide as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

56. **PRO1005**

A cDNA clone (DNA57708-1411) has been identified that encodes a novel polypeptide, designated in the present application as "PRO1005."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1005 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1005 polypeptide having the sequence of amino acid residues from about 21 to about 185, inclusive of Figure 139 (SEQ ID NO:211), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1005 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 90 and about 584, inclusive, of Figure 138 (SEQ ID NO:210). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203021 (DNA57708-1411), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203021 (DNA57708-1411).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 21 to about 185, inclusive of Figure 139 (SEQ ID NO:211), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 50 nucleotides, and preferably at least 100 nucleotides, and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1005 polypeptide having the sequence of amino acid residues from about 21 to about 185, inclusive of Figure 139 (SEQ ID NO:211), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1005 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 139 (SEQ ID NO:211).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to about 185, inclusive of Figure 139 (SEQ ID NO:211), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1005 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1005 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1005 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 21 to 185 of Figure 139 (SEQ ID NO:211).

In another aspect, the invention concerns an isolated PRO1005 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 21 to about 185, inclusive of Figure 139 (SEQ ID NO:211).

In a further aspect, the invention concerns an isolated PRO1005 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to 185 of Figure 139 (SEQ ID NO:211).

In yet another aspect, the invention concerns an isolated PRO1005 polypeptide, comprising the sequence of amino acid residues 21 to about 185, inclusive of Figure 139 (SEQ ID NO:211), or a fragment thereof sufficient to provide a binding site for an anti-PRO1005 antibody. Preferably, the PRO1005 fragment retains a qualitative biological activity of a native PRO1005 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1005 polypeptide having the sequence of amino acid residues from about 21 to about 185, inclusive of Figure 139 (SEQ ID NO:211), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

57. **PRO1073**

A cDNA clone (DNA57710-1451) has been identified that encodes a novel polypeptide, designated in the present application as "PRO1073."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1073 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1073 polypeptide having the sequence of amino acid residues from about 32 to about 299, inclusive of Figure 141 (SEQ ID NO:213), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1073 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 438 and about 1241, inclusive, of Figure 140 (SEQ ID NO:212). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203048 (DNA57710-1451), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203048 (DNA57710-1451).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 32 to about 299, inclusive of Figure 141 (SEQ ID NO:213), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1073 polypeptide having the sequence of amino acid residues from about 32 to about 299, inclusive of Figure 141 (SEQ ID NO:213), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1073 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 31 in the sequence of Figure 141 (SEQ ID NO:213).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 32 to about 299, inclusive of Figure 141 (SEQ ID NO:213), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1073 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1073 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1073 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 32 to 299 of Figure 141 (SEQ ID NO:213).

In another aspect, the invention concerns an isolated PRO1073 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity; more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 32 to about 299, inclusive of Figure 141 (SEQ ID NO:213).

In a further aspect, the invention concerns an isolated PRO1073 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 32 to 299 of Figure 141 (SEQ ID NO:213).

In yet another aspect, the invention concerns an isolated PRO1073 polypeptide, comprising the sequence of amino acid residues 32 to about 299, inclusive of Figure 141 (SEQ ID NO:213), or a fragment thereof sufficient to provide a binding site for an anti-PRO1073 antibody. Preferably, the PRO1073 fragment retains a qualitative biological activity of a native PRO1073 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1073 polypeptide having the sequence of amino acid residues from about 32 to about 299, inclusive of Figure 141 (SEQ ID NO:213), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

58. **PRO1152**

A cDNA clone (DNA57711-1501) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1152".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1152 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1152 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 479, inclusive of Figure 144 (SEQ ID NO:216), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1152 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 58 or about 142 and about 1494, inclusive, of Figure 143 (SEQ ID NO:215). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule

encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203047 (DNA57711-1501) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203047 (DNA57711-1501).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 29 to about 479, inclusive of Figure 144 (SEQ ID NO:216), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 300 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1152 polypeptide having the sequence of amino acid residues from 1 or about 29 to about 479, inclusive of Figure 144 (SEQ ID NO:216), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1152 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 28 in the sequence of Figure 144 (SEQ ID NO:216). The various transmembrane domains have been tentatively identified as extending from about amino acid position 133 to about amino acid position 155, from about amino acid position 168 to about amino acid position 187, from about amino acid position 229 to about amino acid position 247, from about amino acid position 264 to about amino acid position 285, from about amino acid position 309 to about amino acid position 330, from about amino acid position 371 to about amino acid position 390 and from about amino acid position 441 to about amino acid position 464 in the PRO1152 amino acid sequence (Figure 144, SEQ ID NO:216).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 479, inclusive of Figure 144 (SEQ ID NO:216), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1152 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 143 (SEQ ID NO:215).

In another embodiment, the invention provides isolated PRO1152 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1152 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 29 to about 479 of Figure 144 (SEQ ID NO:216).

In another aspect, the invention concerns an isolated PRO1152 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 29 to about 479, inclusive of Figure 144 (SEQ ID NO:216).

In a further aspect, the invention concerns an isolated PRO1152 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 479, inclusive of Figure 144 (SEQ ID NO:216).

In yet another aspect, the invention concerns an isolated PRO1152 polypeptide, comprising the sequence of amino acid residues 1 or about 29 to about 479, inclusive of Figure 144 (SEQ ID NO:216), or a fragment thereof sufficient to provide a binding site for an anti-PRO1152 antibody. Preferably, the PRO1152 fragment retains a qualitative biological activity of a native PRO1152 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1152 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 479, inclusive of Figure 144 (SEQ ID NO:216), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In another embodiment, the invention provides a nucleic aid molecule designated herein as DNA55807 comprising the nucleotide sequence of SEQ ID NO:217 (see Figure 145).

59. **PRO1136**

A cDNA clone (DNA57827-1493) has been identified, having homology to nucleic acid encoding PDZ domain-containing proteins that encodes a novel polypeptide, designated in the present application as "PRO1136".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1136 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1136 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 632, inclusive of Figure 147 (SEQ ID

NO:219), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1136 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 216 or about 261 and about 2111, inclusive, of Figure 146 (SEQ ID NO:218). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203045 (DNA57827-1493) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203045 (DNA57827-1493).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 632, inclusive of Figure 147 (SEQ ID NO:219), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1136 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 632, inclusive of Figure 147 (SEQ ID NO:219), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1136 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 15 in the sequence of Figure 147 (SEQ ID NO:219).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 632, inclusive of Figure 147 (SEQ ID NO:219), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1136 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived

from the nucleotide sequence shown in Figure 146 (SEQ ID NO:218).

In another embodiment, the invention provides isolated PRO1136 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1136 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 16 to about 632 of Figure 147 (SEQ ID NO:219).

In another aspect, the invention concerns an isolated PRO1136 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 632, inclusive of Figure 147 (SEQ ID NO:219).

In a further aspect, the invention concerns an isolated PRO1136 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 632, inclusive of Figure 147 (SEQ ID NO:219).

In yet another aspect, the invention concerns an isolated PRO1136 polypeptide, comprising the sequence of amino acid residues 1 or about 16 to about 632, inclusive of Figure 147 (SEQ ID NO:219), or a fragment thereof sufficient to provide a binding site for an anti-PRO1136 antibody. Preferably, the PRO1136 fragment retains a qualitative biological activity of a native PRO1136 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1136 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 632, inclusive of Figure 147 (SEQ ID NO:219), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1136 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1136 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1136 polypeptide by contacting the native PRO1136 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1136 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

60. PRO813

Applicants have identified a cDNA clone (DNA57834-1339) having homology to pulmonary surfactant-associated protein C that encodes a novel polypeptide, designated in the present application as "PRO813".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO813 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO813 polypeptide having the sequence of amino acid residues from about 1 or about 27 to about 176, inclusive of Figure 149 (SEQ ID NO:221), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO813 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 109 or about 187 and about 636, inclusive, of Figure 148 (SEQ ID NO:220). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209954 (DNA57834-1339). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209954 (DNA57834-1339).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 27 to about 176, inclusive of Figure 149 (SEQ ID NO:221).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO813 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 26 in the sequence of Figure 149 (SEQ ID NO:221).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 27 to about 176, inclusive of Figure 149 (SEQ ID NO:221).

Another embodiment is directed to fragments of a PRO813 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO813 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO813 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 27 to about 176 of Figure 149 (SEQ ID NO:221).

In another aspect, the invention concerns an isolated PRO813 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 27 to about 176, inclusive of Figure 149 (SEQ ID NO:221).

In a further aspect, the invention concerns an isolated PRO813 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 27 to about 176, inclusive of Figure 149 (SEQ ID NO:221).

In yet another aspect, the invention concerns an isolated PRO813 polypeptide, comprising the sequence of amino acid residues 1 or about 27 to about 176, inclusive of Figure 149 (SEQ ID NO:221), or a fragment thereof sufficient to provide a binding site for an anti-PRO813 antibody. Preferably, the PRO813 fragment retains a qualitative biological activity of a native PRO813 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO813 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO813 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO813 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of a native PRO813 polypeptide.

In still a further embodiment, the invention concerns a composition comprising a PRO813 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

61. **PRO809**

A cDNA clone (DNA57836-1338) has been identified, having sequence identity with heparan sulfate proteoglycans, that encodes a novel polypeptide, designated in the present application as "PRO809."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO809 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO809 polypeptide having the sequence of amino acid residues from about 1 or 19 to about 265, inclusive of Figure 151 (SEQ ID NO:223), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-265, or in another embodiment, 19-265.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO809 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 63 or

117 and about 867, inclusive, of Figure 150 (SEQ ID NO:222). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203025 (DNA57836-1338), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203025 (DNA57836-1338).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 19 to about 265, inclusive of Figure 151 (SEQ ID NO:223), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO809 polypeptide having the sequence of amino acid residues from about 1 or 19 to about 265, inclusive of Figure 151 (SEQ ID NO:223), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 19 to about 265, inclusive of Figure 151 (SEQ ID NO:223), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO809 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO809 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 19 through 265 of Figure 151 (SEQ ID NO:223).

In another aspect, the invention concerns an isolated PRO809 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 19 to about 265, inclusive of Figure 151 (SEQ ID NO:223).

In a further aspect, the invention concerns an isolated PRO809 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence

of residues 1 or 19 through 265 of Figure 151 (SEQ ID NO:223).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO809 polypeptide having the sequence of amino acid residues from about 1 or 19 to about 265, inclusive of Figure 151 (SEQ ID NO:223), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO809 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO809 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO809 polypeptide, by contacting the native PRO809 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO809 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

62. **PRO791**

A cDNA clone (DNA57838-1337) has been identified, having sequence identity with MHC class I antigens that encodes a novel polypeptide, designated in the present application as "PRO791."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO791 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO791 polypeptide having the sequence of amino acid residues from about 1 or 26 to about 246, inclusive of Figure 153 (SEQ ID NO:225), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-246, or in another embodiment, 26-246.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO791 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 9 or 84 and about 746, inclusive, of Figure 152 (SEQ ID NO:224). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203014 (DNA57838-1337), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic

acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203014 (DNA57838-1337).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 26 to about 246, inclusive of Figure 153 (SEQ ID NO:225), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO791 polypeptide having the sequence of amino acid residues from about 1 or 26 to about 246, inclusive of Figure 153 (SEQ ID NO:225), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 26 to about 246, inclusive of Figure 153 (SEQ ID NO:225), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO791 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO791 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 26 through 246 of Figure 153 (SEQ ID NO:225).

In another aspect, the invention concerns an isolated PRO791 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 26 to about 246, inclusive of Figure 153 (SEQ ID NO:225).

In a further aspect, the invention concerns an isolated PRO791 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 26 through 246 of Figure 153 (SEQ ID NO:225).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO791 polypeptide having the sequence of amino acid residues from about 1 or 26 to about 246, inclusive of Figure 153 (SEQ ID NO:225), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell

comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO791 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO791 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO791 polypeptide, by contacting the native PRO791 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO791 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

63. **PRO1004**

A cDNA clone (DNA57844-1410) has been identified that encodes a novel polypeptide, designated in the present application as "PRO1004."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1004 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1004 polypeptide having the sequence of amino acid residues from about 25 to about 115, inclusive of Figure 155 (SEQ ID NO:227), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1004 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 191 and about 463, inclusive, of Figure 154 (SEQ ID NO:226). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203010 (DNA57844-1410), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203010 (DNA57844-1410).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 25 to about 115, inclusive of Figure 155 (SEQ ID NO:227), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 50 nucleotides, and preferably at least 100 nucleotides, and produced by hybridizing a test DNA molecule under

stringent conditions with (a) a DNA molecule encoding a PRO1004 polypeptide having the sequence of amino acid residues from about 25 to about 115, inclusive of Figure 155 (SEQ ID NO:227), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1004 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 through about amino acid position 24 in the sequence of Figure 155 (SEQ ID NO:227).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 25 to about 115, inclusive of Figure 155 (SEQ ID NO:227), or (b) the complement of the DNA of (a).

Another embodiment of the invention is directed to fragments of a PRO1004 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1004 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1004 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 25 to 115 of Figure 155 (SEQ ID NO:227).

In another aspect, the invention concerns an isolated PRO1004 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 25 to about 115, inclusive of Figure 155 (SEQ ID NO:227).

In a further aspect, the invention concerns an isolated PRO1004 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 25 to 115 of Figure 155 (SEQ ID NO:227).

In yet another aspect, the invention concerns an isolated PRO1004 polypeptide, comprising the sequence of amino acid residues 25 to about 115, inclusive of Figure 155 (SEQ ID NO:227), or a fragment thereof sufficient to provide a binding site for an anti-PRO1004 antibody. Preferably, the PRO1004 fragment retains a qualitative biological activity of a native PRO1004 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1004 polypeptide having the sequence of amino acid residues from about 25 to about 115, inclusive of Figure 155 (SEQ ID NO:227), or (b)

the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

64. **PRO1111**

A cDNA clone (DNA58721-1475) has been identified that encodes a novel polypeptide having sequence identity with LIG and designated in the present application as "PRO1111."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1111 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1111 polypeptide having the sequence of amino acid residues from about 1 to about 653, inclusive of Figure 157 (SEQ ID NO:229), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1111 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 57 and about 2015, inclusive, of Figure 156 (SEQ ID NO:228). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203110 (DNA58721-1475), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203110 (DNA58721-1475).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 653, inclusive of Figure 157 (SEQ ID NO:229), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1111 polypeptide having the sequence of amino acid residues from about 1 to about 653, inclusive of Figure 157 (SEQ ID NO:229), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most

preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1111 polypeptide in its soluble form, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains has been tentatively identified as extending from about amino acid positions 21-40 (type II) and 528-548 in the PRO1111 amino acid sequence (Figure 157, SEQ ID NO:229).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 653, inclusive of Figure 157 (SEQ ID NO:229), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1111 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1111 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1111 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 653 of Figure 157 (SEQ ID NO:229).

In another aspect, the invention concerns an isolated PRO1111 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 653, inclusive of Figure 157 (SEQ ID NO:229).

In a further aspect, the invention concerns an isolated PRO1111 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 through 653 of Figure 157 (SEQ ID NO:229).

In yet another aspect, the invention concerns an isolated PRO1111 polypeptide, comprising the sequence of amino acid residues 1 to about 653, inclusive of Figure 157 (SEQ ID NO:229), or a fragment thereof sufficient to provide a binding site for an anti-PRO1111 antibody. Preferably, the PRO1111 fragment retains a qualitative biological activity of a native PRO1111 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1111 polypeptide having the sequence of amino acid residues from about 1 to about 653, inclusive of Figure 157 (SEQ ID NO:229), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising

the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1111 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1111 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1111 polypeptide, by contacting the native PRO1111 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1111 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

65. **PRO1344**

A cDNA clone (DNA58723-1588) has been identified, having homology to nucleic acid encoding factor C that encodes a novel polypeptide, designated in the present application as "PRO1344".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1344 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1344 polypeptide having the sequence of amino acid residues from about 1 or about 24 to about 720, inclusive of Figure 159 (SEQ ID NO:231), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1344 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 26 or about 95 and about 2185, inclusive, of Figure 158 (SEQ ID NO:230). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203133 (DNA58723-1588) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203133 (DNA58723-1588).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 24 to about 720, inclusive of Figure 159 (SEQ ID NO:231), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA

molecule encoding a PRO1344 polypeptide having the sequence of amino acid residues from 1 or about 24 to about 720, inclusive of Figure 159 (SEQ ID NO:231), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1344 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 23 in the sequence of Figure 159 (SEQ ID NO:231).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 24 to about 720, inclusive of Figure 159 (SEQ ID NO:231), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1344 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 158 (SEQ ID NO:230).

In another embodiment, the invention provides isolated PRO1344 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1344 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 24 to about 720 of Figure 159 (SEQ ID NO:231).

In another aspect, the invention concerns an isolated PRO1344 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 24 to about 720, inclusive of Figure 159 (SEQ ID NO:231).

In a further aspect, the invention concerns an isolated PRO1344 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 24 to about 720, inclusive of Figure 159 (SEQ ID NO:231).

In yet another aspect, the invention concerns an isolated PRO1344 polypeptide, comprising the sequence of amino acid residues 1 or about 24 to about 720, inclusive of Figure 159 (SEQ ID NO:231), or a fragment thereof sufficient to provide a binding site for an anti-PRO1344 antibody. Preferably, the PRO1344 fragment retains a qualitative biological activity of a native PRO1344 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1344 polypeptide having the sequence of amino acid residues from about 1 or about 24 to about 720, inclusive of Figure 159 (SEQ ID NO:231), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1344 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1344 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1344 polypeptide by contacting the native PRO1344 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1344 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

66. **PRO1109**

A cDNA clone (DNA58737-1473) has been identified, having homology to nucleic acid encoding β-1,4-galactosyltransferase, that encodes a novel polypeptide, designated in the present application as "PRO1109".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1109 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1109 polypeptide having the sequence of amino acid residues from about 1 or about 28 to about 344, inclusive of Figure 161 (SEQ ID NO:236), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1109 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 119 or about 200 and about 1150, inclusive, of Figure 160 (SEQ ID NO:235). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203136 (DNA58737-1473) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203136 (DNA58737-1473).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 28 to about 344, inclusive of Figure 161 (SEQ ID NO:236), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1109 polypeptide having the sequence of amino acid residues from 1 or about 28 to about 344, inclusive of Figure 161 (SEQ ID NO:236), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1109 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 27 in the sequence of Figure 161 (SEQ ID NO:236).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 28 to about 344, inclusive of Figure 161 (SEQ ID NO:236), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1109 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 160 (SEQ ID NO:235).

In another embodiment, the invention provides isolated PRO1109 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1109 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 28 to about 344 of Figure 161 (SEQ ID NO:236).

In another aspect, the invention concerns an isolated PRO1109 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 28 to about 344, inclusive of Figure 161 (SEQ ID NO:236).

In a further aspect, the invention concerns an isolated PRO1109 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least

about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 28 to about 344, inclusive of Figure 161 (SEQ ID NO:236).

In yet another aspect, the invention concerns an isolated PRO1109 polypeptide, comprising the sequence of amino acid residues 1 or about 28 to about 344, inclusive of Figure 161 (SEQ ID NO:236), or a fragment thereof sufficient to provide a binding site for an anti-PRO1109 antibody. Preferably, the PRO1109 fragment retains a qualitative biological activity of a native PRO1109 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1109 polypeptide having the sequence of amino acid residues from about 1 or about 28 to about 344, inclusive of Figure 161 (SEQ ID NO:236), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1109 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1109 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1109 polypeptide by contacting the native PRO1109 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1109 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

67. **PRO1383**

A cDNA clone (DNA58743-1609) has been identified, having homology to nucleic acid encoding the human melanoma cell-expressed protein nmb, that encodes a novel polypeptide, designated in the present application as "PRO1383".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1383 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1383 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 423, inclusive of Figure 163 (SEQ ID NO:241), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1383 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 122 or about 194 and about 1390, inclusive, of Figure 162 (SEQ ID NO:240). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203154 (DNA58743-1609) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203154 (DNA58743-1609).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 423, inclusive of Figure 163 (SEQ ID NO:241), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1383 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 423, inclusive of Figure 163 (SEQ ID NO:241), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1383 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 24 in the sequence of Figure 163 (SEQ ID NO:241). The transmembrane domain has been tentatively identified as extending from about amino acid position 339 to about amino acid position 362 in the PRO1383 amino acid sequence (Figure 163, SEQ ID NO:241).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 423, inclusive of Figure 163 (SEQ ID NO:241), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1383 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 162 (SEQ ID NO:240).

In another embodiment, the invention provides isolated PRO1383 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1383 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 25 to about 423 of Figure 163 (SEQ ID NO:241).

In another aspect, the invention concerns an isolated PRO1383 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 423, inclusive of Figure 163 (SEQ ID NO:241).

In a further aspect, the invention concerns an isolated PRO1383 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 423, inclusive of Figure 163 (SEQ ID NO:241).

In yet another aspect, the invention concerns an isolated PRO1383 polypeptide, comprising the sequence of amino acid residues 1 or about 25 to about 423, inclusive of Figure 163 (SEQ ID NO:241), or a fragment thereof sufficient to provide a binding site for an anti-PRO1383 antibody. Preferably, the PRO1383 fragment retains a qualitative biological activity of a native PRO1383 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1383 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 423, inclusive of Figure 163 (SEQ ID NO:241), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1383 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1383 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1383 polypeptide by contacting the native PRO1383 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1383 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

68. **PRO1003**

Applicants have identified a cDNA clone, DNA58846-1409, that encodes a novel secreted polypeptide wherein the polypeptide is designated in the present application as "PRO1003".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1003 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most

preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1003 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 84, inclusive of Figure 165 (SEQ ID NO:246), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1003 polypeptide comprising DNA that hybridizes to the complement of the nucleic acid between about residues 41 or about 113 and about 292 inclusive of Figure 164 (SEQ ID NO:245). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209957 (DNA58846-1409), which was deposited on June 9, 1998. In a preferred embodiment, the nucleic acid comprises a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209957 (DNA58846-1409).

In an additional aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 84, inclusive of Figure 165 (SEQ ID NO:246).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 84, inclusive of Figure 165 (SEQ ID NO:246).

Another embodiment is directed to fragments of a PRO1003 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1003 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1003 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 25 to 84 of Figure 165 (SEQ ID NO:246).

In another aspect, the invention concerns an isolated PRO1003 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to 84, inclusive of Figure 165 (SEQ ID NO:246).

In a further aspect, the invention concerns an isolated PRO1003 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least

about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 84 of Figure 165 (SEQ ID NO:246).

In yet another aspect, the invention concerns an isolated PRO1003 polypeptide, comprising the sequence of amino acid residues 1 or about 25 to about 84, inclusive of Figure 165 (SEQ ID NO:246), or a fragment thereof sufficient to provide a binding site for an anti-PRO1003 antibody. Preferably, the PRO1003 fragment retains a qualitative biological activity of a native PRO1003 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1003 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

69. **PRO1108**

Applicants have identified a cDNA clone (DNA58848-1472) having homology to nucleic acid encoding the LPAAT protein that encodes a novel polypeptide, designated in the present application as "PRO1108".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1108 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1108 polypeptide having the sequence of amino acid residues from about 1 to about 456, inclusive of Figure 167 (SEQ ID NO:248), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1108 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 77 and about 1444, inclusive, of Figure 166 (SEQ ID NO:247). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209955 (DNA58848-1472). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209955 (DNA58848-1472).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 456, inclusive of Figure 167 (SEQ ID NO:248).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1108 polypeptide, with or without the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains have been tentatively identified as being type II domains extending from about amino acid position 22 to about amino acid position 42, from about amino acid position 156 to about amino acid position 176, from

about amino acid position 180 to about amino acid position 199 and from about amino acid position 369 to about amino acid position 388 in the PRO1108 amino acid sequence (Figure 167, SEQ ID NO:248).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 456, inclusive of Figure 167 (SEQ ID NO:248).

Another embodiment is directed to fragments of a PRO1108 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1108 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1108 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to about 456 of Figure 167 (SEQ ID NO:248).

In another aspect, the invention concerns an isolated PRO1108 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 456, inclusive of Figure 167 (SEQ ID NO:248).

In a further aspect, the invention concerns an isolated PRO1108 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 456, inclusive of Figure 167 (SEQ ID NO:248).

In yet another aspect, the invention concerns an isolated PRO1108 polypeptide, comprising the sequence of amino acid residues 1 to about 456, inclusive of Figure 167 (SEQ ID NO:248), or a fragment thereof sufficient to provide a binding site for an anti-PRO1108 antibody. Preferably, the PRO1108 fragment retains a qualitative biological activity of a native PRO1108 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1108 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1108 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1108 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of a native PRO1108 polypeptide.

In still a further embodiment, the invention concerns a composition comprising a PRO1108 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

70. **PRO1137**

Applicants have identified a cDNA clone, DNA58849-1494, that encodes a novel polypeptide having homology to ribosyltransferase wherein the polypeptide is designated in the present application as "PRO1137".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1137 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1137 polypeptide having the sequence of amino acid residues from 1 or about 15 to about 240, inclusive of Figure 169 (SEQ ID NO:250), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1137 polypeptide comprising DNA that hybridizes to the complement of the nucleic acid sequence having about residues 77 or about 119 to about 796, inclusive of Figure 168 (SEQ ID NO:249). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209958 (DNA58849-1494), which was deposited on June 9, 1998, or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209958 (DNA58849-1494).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 15 to about 240, inclusive of Figure 169 (SEQ ID NO:250).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1137 polypeptide with or without the N-terminal signal sequence and/or the initiating methionine, or the complement of such encoding DNA molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 14 in the sequence of Figure 169 (SEQ ID NO:250).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 90% positives, and most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 15 to about 240, inclusive of Figure 169 (SEQ ID NO:250).

Another embodiment is directed to fragments of a PRO1137 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50

nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1137 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1137 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 15 to 240 of Figure 169 (SEQ ID NO:250).

In another aspect, the invention concerns an isolated PRO1137 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 15 to 240, inclusive of Figure 169 (SEQ ID NO:250).

In a further aspect, the invention concerns an isolated PRO1137 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, and most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 15 to about 240 of Figure 169 (SEQ ID NO:250).

In yet another aspect, the invention concerns an isolated PRO1137 polypeptide, comprising the sequence of amino acid residues 1 or about 15 to about 240, inclusive of Figure 169 (SEQ ID NO:250), or a fragment thereof sufficient to provide a binding site for an anti-PRO1137 antibody. Preferably, the PRO1137 fragment retains a qualitative biological activity of a native PRO1137 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1137 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

In yet another embodiment, the invention concerns agonist and antagonists of the PRO1137 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1137 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of a native PRO1137 polypeptide.

In still a further embodiment, the invention concerns a composition comprising a PRO1137 polypeptide as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

71. <u>PRO1138</u>

Applicants have identified a cDNA clone, DNA58850-1495, that encodes a novel polypeptide having homology to CD84 leukocyte antigen wherein the polypeptide is designated in the present application as "PRO1138".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1138 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1138 polypeptide having the sequence of amino acid residues from 1 or about 23 to about 335, inclusive of Figure 171 (SEQ ID NO:253), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1138 polypeptide comprising DNA that hybridizes to the complement of the nucleic acid sequence having about residues 38 or about 104 to about 1042, inclusive of Figure 170 (SEQ ID NO:252). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209956 (DNA58850-1495), which was deposited on June 9, 1998, or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209956 (DNA58850-1495).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 23 to about 335, inclusive of Figure 171 (SEQ ID NO:253).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1138 extracellular domain (ECD), with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble variants (i.e. transmembrane domain(s) deleted or inactivated) or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 to about amino acid position 22 in the sequence of Figure 171 (SEQ ID NO:253). A transmembrane domain region has been tentatively identified as extending from about amino acid position 224 to about amino acid position 250 in the PRO1138 amino acid sequence (Figure 171, SEQ ID NO:253).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 90% positives, and most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 23 to about 335, inclusive of Figure 171 (SEQ ID NO:253).

Another embodiment is directed to fragments of a PRO1138 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1138 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1138 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 23 to 335 of Figure 171 (SEQ ID NO:253).

In another aspect, the invention concerns an isolated PRO1138 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more

preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 23 to 335, inclusive of Figure 171 (SEQ ID NO:253).

In a further aspect, the invention concerns an isolated PRO1138 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, and most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 23 to about 335 of Figure 171 (SEQ ID NO:253).

In another aspect, the invention concerns a PRO1138 extracellular domain comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 23 to X of Figure 171 (SEQ ID NO:253), wherein X is any one of amino acid residues 219 to 228 of Figure 171 (SEQ ID NO:253).

In yet another aspect, the invention concerns an isolated PRO1138 polypeptide, comprising the sequence of amino acid residues 1 or about 23 to about 335, inclusive of Figure 171 (SEQ ID NO:253), or a fragment thereof sufficient to provide a binding site for an anti-PRO1138 antibody. Preferably, the PRO1138 fragment retains a qualitative biological activity of a native PRO1138 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1138 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

In yet another embodiment, the invention concerns agonist and antagonists of the PRO1138 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1138 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of a native PRO1138 polypeptide.

In still a further embodiment, the invention concerns a composition comprising a PRO1138 polypeptide as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

In another embodiment, the invention provides a nucleotide sequence designated herein as DNA49140 comprising the nucleotide sequence of Figure 172 (SEQ ID NO:254).

72. **PRO1054**

A cDNA clone (DNA58853-1423) has been identified, having homology to nucleic acid encoding majaor urinary proteins (MUPs) that encodes a novel polypeptide, designated in the present application as "PRO1054".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1054 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1054 polypeptide having the sequence of amino acid residues from about 1 or about 19 to about 180, inclusive of Figure 174 (SEQ ID NO:256), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1054 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 46

or about 100 and about 585, inclusive, of Figure 173 (SEQ ID NO:255). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203016 (DNA58853-1423) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203016 (DNA58853-1423).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 19 to about 180, inclusive of Figure 174 (SEQ ID NO:256), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1054 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 180, inclusive of Figure 174 (SEQ ID NO:256), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1054 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 18 in the sequence of Figure 174 (SEQ ID NO:256).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 19 to about 180, inclusive of Figure 174 (SEQ ID NO:256), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1054 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 173 (SEQ ID NO:255).

In another embodiment, the invention provides isolated PRO1054 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1054 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 19 to about 180 of Figure 174 (SEQ ID NO:256).

In another aspect, the invention concerns an isolated PRO1054 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 19 to about 180, inclusive of Figure 174 (SEQ ID NO:256).

In a further aspect, the invention concerns an isolated PRO1054 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 19 to about 180, inclusive of Figure 174 (SEQ ID NO:256).

In yet another aspect, the invention concerns an isolated PRO1054 polypeptide, comprising the sequence of amino acid residues 1 or about 19 to about 180, inclusive of Figure 174 (SEQ ID NO:256), or a fragment thereof sufficient to provide a binding site for an anti-PRO1054 antibody. Preferably, the PRO1054 fragment retains a qualitative biological activity of a native PRO1054 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1054 polypeptide having the sequence of amino acid residues from about 1 or about 19 to about 180, inclusive of Figure 174 (SEQ ID NO:256), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1054 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1054 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1054 polypeptide by contacting the native PRO1054 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1054 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

73. PRO994

A cDNA clone (DNA58855-1422) has been identified, having homology to nucleic acid encoding the tumor-associated antigen L6 that encodes a novel polypeptide, designated in the present application as "PRO994".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO994 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO994 polypeptide having the sequence of amino acid residues from about 1 to about 229, inclusive of Figure 176 (SEQ ID NO:258), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO994 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 31 and about 717, inclusive, of Figure 175 (SEQ ID NO:257). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203018 (DNA58855-1422) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203018 (DNA58855-1422).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 229, inclusive of Figure 176 (SEQ ID NO:258), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO994 polypeptide having the sequence of amino acid residues from 1 to about 229, inclusive of Figure 176 (SEQ ID NO:258), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO994 polypeptide, with or without the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The multiple transmembrane domains have been tentatively identified as extending from about amino acid position 10 to about amino acid position 31, from about amino acid position 50 to about amino acid position 72, from about amino acid position 87 to about amino acid position 110 and from about amino acid position 191 to about amino acid position 213 in the PRO994 amino acid sequence (Figure 176, SEQ ID NO:258).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the

amino acid sequence of residues 1 to about 229, inclusive of Figure 176 (SEQ ID NO:258), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO994 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 175 (SEQ ID NO:257).

In another embodiment, the invention provides isolated PRO994 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO994 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 229 of Figure 176 (SEQ ID NO:258).

In another aspect, the invention concerns an isolated PRO994 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 229, inclusive of Figure 176 (SEQ ID NO:258).

In a further aspect, the invention concerns an isolated PRO994 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 229, inclusive of Figure 176 (SEQ ID NO:258).

In yet another aspect, the invention concerns an isolated PRO994 polypeptide, comprising the sequence of amino acid residues 1 to about 229, inclusive of Figure 176 (SEQ ID NO:258), or a fragment thereof sufficient to provide a binding site for an anti-PRO994 antibody. Preferably, the PRO994 fragment retains a qualitative biological activity of a native PRO994 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO994 polypeptide having the sequence of amino acid residues from about 1 to about 229, inclusive of Figure 176 (SEQ ID NO:258), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO994 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO994 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO994 polypeptide by contacting the native PRO994 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO994 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

74. **PRO812**

A cDNA clone (DNA59205-1421) has been identified, having homology to nucleic acid encoding prostatic steroid-binding protein c1 that encodes a novel polypeptide, designated in the present application as "PRO812".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO812 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO812 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 83, inclusive of Figure 178 (SEQ ID NO:260), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO812 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 55 or about 100 and about 303, inclusive, of Figure 177 (SEQ ID NO:259). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203009 (DNA59205-1421) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203009 (DNA59205-1421).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 83, inclusive of Figure 178 (SEQ ID NO:260), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO812 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 83, inclusive of Figure 178 (SEQ ID NO:260), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO812 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 15 in the sequence of Figure 178 (SEQ ID NO:260).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 83, inclusive of Figure 178 (SEQ ID NO:260), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO812 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 177 (SEQ ID NO:259).

In another embodiment, the invention provides isolated PRO812 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO812 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 16 to about 83 of Figure 178 (SEQ ID NO:260).

In another aspect, the invention concerns an isolated PRO812 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 83, inclusive of Figure 178 (SEQ ID NO:260).

In a further aspect, the invention concerns an isolated PRO812 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 83, inclusive of Figure 178 (SEQ ID NO:260).

In yet another aspect, the invention concerns an isolated PRO812 polypeptide, comprising the sequence of amino acid residues 1 or about 16 to about 83, inclusive of Figure 178 (SEQ ID NO:260), or a fragment thereof sufficient to provide a binding site for an anti-PRO812 antibody. Preferably, the PRO812 fragment retains a qualitative biological activity of a native PRO812 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO812 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 83, inclusive of Figure 178 (SEQ ID NO:260), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host

cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO812 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO812 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO812 polypeptide by contacting the native PRO812 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO812 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

75. **PRO1069**

Applicants have identified a cDNA clone, DNA59211-1450, that encodes a novel polypeptide having homology to CHIF wherein the polypeptide is designated in the present application as "PRO1069".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1069 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1069 polypeptide having the sequence of amino acid residues from 1 or about 17 to about 89, inclusive of Figure 180 (SEQ ID NO:262), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1069 polypeptide comprising DNA that hybridizes to the complement of the nucleic acid sequence having about residues 197 or about 245 to about 463, inclusive of Figure 179 (SEQ ID NO:261). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209960 (DNA59211-1450), which was deposited on June 9, 1998. In a preferred embodiment, the nucleic acid comprises a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209960 (DNA59211-1450).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 17 to about 89, inclusive of Figure 180 (SEQ ID NO:262).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1069 extracellular domain (ECD), with or without the N-terminal signal sequence and/or the initiating

methionine, and its soluble variants (i.e. transmembrane domain(s) deleted or inactivated) or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 to about amino acid position 16 in the sequence of Figure 180 (SEQ ID NO:262). A transmembrane domain region has been tentatively identified as extending from about amino acid position 36 to about amino acid position 59 in the PRO1069 amino acid sequence (Figure 180, SEQ ID NO:262).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 17 to about 89, inclusive of Figure 180 (SEQ ID NO:262).

Another embodiment is directed to fragments of a PRO1069 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1069 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1069 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 17 to 89 of Figure 180 (SEQ ID NO:262).

In another aspect, the invention concerns an isolated PRO1069 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 17 to 89, inclusive of Figure 180 (SEQ ID NO:262).

In a further aspect, the invention concerns an isolated PRO1069 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 17 to about 89 of Figure 180 (SEQ ID NO:262).

In another aspect, the invention concerns a PRO1069 extracellular domain comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 17 to X of Figure 180 (SEQ ID NO:262), wherein X is any one of amino acid residues 32 to 41 of Figure 180 (SEQ ID NO:262).

In yet another aspect, the invention concerns an isolated PRO1069 polypeptide, comprising the sequence of amino acid residues 1 or about 17 to about 89, inclusive of Figure 180 (SEQ ID NO:262), or a fragment thereof sufficient to provide a binding site for an anti-PRO1069 antibody. Preferably, the PRO1069 fragment retains a qualitative biological activity of a native PRO1069 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1069 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

In yet another embodiment, the invention concerns agonist and antagonists of the PRO1069 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1069 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of a native PRO1069 polypeptide.

In still a further embodiment, the invention concerns a composition comprising a PRO1069 polypeptide as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

76. PRO1129

Applicants have identified a cDNA clone (DNA59213-1487) having homology to nucleic acid encoding cytochrome P-450 family members that encodes a novel polypeptide, designated in the present application as "PRO1129".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1129 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1129 polypeptide having the sequence of amino acid residues from about 1 to about 524, inclusive of Figure 182 (SEQ ID NO:264), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1129 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 42 and about 1613, inclusive, of Figure 181 (SEQ ID NO:263). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209959 (DNA59213-1487). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209959 (DNA59213-1487).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 524, inclusive of Figure 182 (SEQ ID NO:264).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1129 polypeptide, with or without the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The type II transmembrane domains have been tentatively identified as extending from about amino acid position 13 to about amino acid position 32 and from about amino acid position 77 to about amino acid position 102 in the PRO1129 amino acid sequence (Figure 182, SEQ ID NO:264).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 524, inclusive of Figure 182 (SEQ ID NO:264).

Another embodiment is directed to fragments of a PRO1129 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1129 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1129 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to about 524 of Figure 182 (SEQ ID NO:264).

In another aspect, the invention concerns an isolated PRO1129 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 524, inclusive of Figure 182 (SEQ ID NO:264).

In a further aspect, the invention concerns an isolated PRO1129 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 524, inclusive of Figure 182 (SEQ ID NO:264).

In yet another aspect, the invention concerns an isolated PRO1129 polypeptide, comprising the sequence of amino acid residues 1 to about 524, inclusive of Figure 182 (SEQ ID NO:264), or a fragment thereof sufficient to provide a binding site for an anti-PRO1129 antibody. Preferably, the PRO1129 fragment retains a qualitative biological activity of a native PRO1129 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1129 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1129 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1129 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of a native PRO1129 polypeptide.

In still a further embodiment, the invention concerns a composition comprising a PRO1129 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

77. **PRO1068**

A cDNA clone (DNA59214-1449) has been identified, that encodes a novel polypeptide having homology to urotensin and designated the present application as "PRO1068."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1068 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1068 polypeptide having the sequence of amino acid residues from about 21 to about 124, inclusive of Figure 184 (SEQ ID NO:266), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1068 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 102 and about 413, inclusive, of Figure 183 (SEQ ID NO:265). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203046 (DNA59214-1449), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203046 (DNA59214-1449).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 21 to about 124, inclusive of Figure 184 (SEQ ID NO:266), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1068 polypeptide having the sequence of amino acid residues from about 21 to about 124, inclusive of Figure 184 (SEQ ID NO:266), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1068 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 184 (SEQ ID NO:266).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the

amino acid sequence of residues 21 to about 124, inclusive of Figure 184 (SEQ ID NO:266), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1068 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1068 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1068 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 21 to 124 of Figure 184 (SEQ ID NO:266).

In another aspect, the invention concerns an isolated PRO1068 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 21 to about 124, inclusive of Figure 184 (SEQ ID NO:266).

In a further aspect, the invention concerns an isolated PRO1068 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to 124 of Figure 184 (SEQ ID NO:266).

In yet another aspect, the invention concerns an isolated PRO1068 polypeptide, comprising the sequence of amino acid residues 21 to about 124, inclusive of Figure 184 (SEQ ID NO:266), or a fragment thereof sufficient to provide a binding site for an anti-PRO1068 antibody. Preferably, the PRO1068 fragment retains a qualitative biological activity of a native PRO1068 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1068 polypeptide having the sequence of amino acid residues from about 21 to about 124, inclusive of Figure 184 (SEQ ID NO:266), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1068 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1068 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1068 polypeptide, by contacting the native PRO1068 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1068 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

78. **PRO1066**

Applicants have identified a cDNA clone (DNA59215-1425) that encodes a novel secreted polypeptide, designated in the present application as "PRO1066".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1066 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1066 polypeptide having the sequence of amino acid residues from about 1 or about 24 to about 117, inclusive of Figure 186 (SEQ ID NO:268), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1066 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 176 or about 245 and about 527, inclusive, of Figure 185 (SEQ ID NO:267). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209961 (DNA59215-1425). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209961 (DNA59215-1425).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 24 to about 117, inclusive of Figure 186 (SEQ ID NO:268).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1066 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 23 in the sequence of Figure 186 (SEQ ID NO:268).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 24 to about 117, inclusive of Figure 186 (SEQ ID NO:268).

Another embodiment is directed to fragments of a PRO1066 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1066 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1066 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 24 to about 117 of Figure 186 (SEQ ID NO:268).

In another aspect, the invention concerns an isolated PRO1066 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 24 to about 117, inclusive of Figure 186 (SEQ ID NO:268).

In a further aspect, the invention concerns an isolated PRO1066 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 24 to about 117, inclusive of Figure 186 (SEQ ID NO:268).

In yet another aspect, the invention concerns an isolated PRO1066 polypeptide, comprising the sequence of amino acid residues 1 or about 24 to about 117, inclusive of Figure 186 (SEQ ID NO:268), or a fragment thereof sufficient to provide a binding site for an anti-PRO1066 antibody. Preferably, the PRO1066 fragment retains a qualitative biological activity of a native PRO1066 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1066 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

79. **PRO1184**

Applicants have identified a cDNA clone (DNA59220-1514) that encodes a novel secreted polypeptide, designated in the present application as "PRO1184".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1184 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1184 polypeptide having the sequence of amino acid residues from 1 or about 39 through 142 of Figure 188 (SEQ ID NO:270), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1184 polypeptide comprising DNA hybridizing to the complement of the nucleic acid at about residues 106 or 220 through 531 of SEQ ID NO:269. In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1184 polypeptide comprising DNA hybridizing to the complement of the nucleic of SEQ ID NO:269. Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule

encoding the same mature polypeptide encoded by the human protein cDNA in ATCC of DNA59220-1514. In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit of DNA59220-1514.

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 39 through 142 of SEQ ID NO:270.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1184 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble variants, or is complementary to such an encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 to about amino acid position 38 of SEQ ID NO:270.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 39 through 142 of SEQ ID NO:270.

Another embodiment is directed to fragments of a PRO1184 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1184 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1184 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 39 through 142 of SEQ ID NO:270.

In another aspect, the invention concerns an isolated PRO1184 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 39 through 142 of SEQ ID NO:270.

In a further aspect, the invention concerns an isolated PRO1184 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 39 through 142 of SEQ ID NO:270.

In yet another aspect, the invention concerns an isolated PRO1184 polypeptide, comprising the sequence of amino acid residues 1 or about 39 through 142 of SEQ ID NO:270, or a fragment thereof sufficient to provide a binding site for an anti-PRO1184 antibody. Preferably, the PRO1184 fragment retains a qualitative biological activity of a native PRO1184 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1184 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

80. PRO1360

A cDNA clone (DNA59488-1603) has been identified that encodes a novel polypeptide designated in the present application as "PRO1360."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1360 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1360 polypeptide having the sequence of amino acid residues from about 30 to about 285, inclusive of Figure 190 (SEQ ID NO:272), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1360 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 140 and about 908, inclusive, of Figure 189 (SEQ ID NO:271). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203157 (DNA59488-1603), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203157 (DNA59488-1603).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 30 to about 285, inclusive of Figure 190 (SEQ ID NO:272), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1360 polypeptide having the sequence of amino acid residues from about 30 to about 285, inclusive of Figure 190 (SEQ ID NO:272), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more

preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 30 to about 285, inclusive of Figure 190 (SEQ ID NO:272), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1360 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1360 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1360 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 30 through 285 of Figure 190 (SEQ ID NO:272).

In another aspect, the invention concerns an isolated PRO1360 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 30 to about 285, inclusive of Figure 190 (SEQ ID NO:272).

In a further aspect, the invention concerns an isolated PRO1360 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 30 through 285 of Figure 190 (SEQ ID NO:272).

In yet another aspect, the invention concerns an isolated PRO1360 polypeptide, comprising the sequence of amino acid residues 30 to about 285, inclusive of Figure 190 (SEQ ID NO:272), or a fragment thereof sufficient to provide a binding site for an anti-PRO1360 antibody. Preferably, the PRO1360 fragment retains a qualitative biological activity of a native PRO1360 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1360 polypeptide having the sequence of amino acid residues from about 30 to about 285, inclusive of Figure 190 (SEQ ID NO:272), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1360 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1360 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1360 polypeptide, by contacting the native PRO1360 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1360 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

81. **PRO1029**

A cDNA clone (DNA59493-1420) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO1029".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1029 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1029 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 86, inclusive of Figure 192 (SEQ ID NO:274), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1029 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 39 or about 96 and about 296, inclusive, of Figure 191 (SEQ ID NO:274). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203050 (DNA59493-1420) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203050 (DNA59493-1420).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 20 to about 86, inclusive of Figure 192 (SEQ ID NO:274), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1029 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 86, inclusive of Figure 192 (SEQ ID NO:274), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1029 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is

complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 19 in the sequence of Figure 192 (SEQ ID NO:274).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 20 to about 86, inclusive of Figure 192 (SEQ ID NO:274), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1029 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 191 (SEQ ID NO:273).

In another embodiment, the invention provides isolated PRO1029 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1029 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 20 to about 86 of Figure 192 (SEQ ID NO:274).

In another aspect, the invention concerns an isolated PRO1029 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 20 to about 86, inclusive of Figure 192 (SEQ ID NO:274).

In a further aspect, the invention concerns an isolated PRO1029 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 20 to about 86, inclusive of Figure 192 (SEQ ID NO:274).

In yet another aspect, the invention concerns an isolated PRO1029 polypeptide, comprising the sequence of amino acid residues 1 or about 20 to about 86, inclusive of Figure 192 (SEQ ID NO:274), or a fragment thereof sufficient to provide a binding site for an anti-PRO1029 antibody. Preferably, the PRO1029 fragment retains a qualitative biological activity of a native PRO1029 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1029 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 86, inclusive of Figure 192 (SEQ ID NO:274), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

82. **PRO1139**

Applicants have identified a novel cDNA clone (DNA59497-1496) that encodes a novel human protein originally designated as PRO1139.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1139 polypeptide having the sequence of amino acid residues from about 29 to about 131 of Figure 194 (SEQ ID NO:276), or (b) the complement of the DNA molecule of (a).

In another embodiment, the invention concerns an isolated nucleic acid molecule comprising DNA hybridizing to the complement of the polynucleotide sequence between about residues 80 and 391, inclusive, of Figure 193 (SEQ ID NO:275). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further embodiment, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209941 (DNA59497-1496). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209941 (DNA59497-1496).

In a still further embodiment, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 29 to about 131 of Figure 194 (SEQ ID NO:276).

In a specific embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a native or variant PRO1139 polypeptide, with or without the N-terminal signal sequence, and with or without the transmembrane regions which have been identified as stretching from about amino acid position 33 to about amino acid position 52; from about amino acid position 71 to about amino acid position 89; and from about amino acid position 98 to about amino acid position 120, respectively of the amino acid sequence of Figure 194, SEQ ID NO:276. In one aspect, the isolated nucleic acid comprises DNA encoding a mature, full-length native PRO1139 polypeptide having amino acid residues 1 to 131 of Figure 194, SEQ ID NO:276, or is complementary to such encoding nucleic acid sequence.

In another embodiment, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues from about 29 to about 131 of Figure 194 (SEQ ID NO:276).

In another embodiment, the invention provides isolated PRO1139 polypeptides. In particular, the invention provides isolated native sequence PRO1139 polypeptide, which in one embodiment, include the amino acid sequence comprising residues 29 to 131 of Figure 194 (SEQ ID NO:276). The invention also provides for variants of the PRO1139 polypeptide which are encoded by any of the isolated nucleic acid molecules

hereinabove defined. Specific variants include, but are not limited to, deletion (truncated) variants of the full-length native sequence PRO1139 which lack the N-terminal signal sequence and/or have at least one transmembrane domain deleted or inactivated. The variants specifically include variants of the full-length mature polypeptide of Figure 194 (SEQ ID NO:276) in which one or more of the transmembrane regions between amino acid residues 33-52, 71-8, and 98-120, respectively have been deleted or inactivated, and which may additionally have the N-terminal signal sequence (amino acid residues 1-28) and/or the initiating methionine deleted.

In a further embodiment, the invention concerns an isolated PRO1139 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues from about 29 to about 131 of Figure 194 (SEQ ID NO:276).

In yet another aspect, the invention concerns an isolated PRO1139 polypeptide, comprising the sequence of amino acid residues 29 to about 131, inclusive of Figure 194 (SEQ ID NO:276) or a fragment thereof sufficient to provide a binding site for an anti-PRO1139 antibody. Preferably, the PRO1139 fragment retains a qualitative biological activity of a native PRO1139 polypeptide.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1139 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1139 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of a native PRO1139 polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1139 polypeptide (including variants), or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

The invention also concerns a method of treating obesity comprising administering to a patient an effective amount of an antagonist of a PRO1139 polypeptide. In a specific embodiment, the antagonist is a blocking antibody specifically binding a native PRO1139 polypeptide.

83. <u>PRO1309</u>

A cDNA clone (DNA59588-1571) has been identified that encodes a novel polypeptide having leucine rich repeats and designated in the present application as "PRO1309."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1309 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1309 polypeptide having the sequence of amino acid residues from about 35 to about 522, inclusive of Figure 196 (SEQ ID NO:278), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1309 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 822 and about 2285, inclusive, of Figure 195 (SEQ ID NO:277). Preferably, hybridization occurs under stringent

hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203106 (DNA59588-1571), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203106 (DNA59588-1571).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 35 to about 522, inclusive of Figure 196 (SEQ ID NO:278), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1309 polypeptide having the sequence of amino acid residues from about 35 to about 522, inclusive of Figure 196 (SEQ ID NO:278), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1309 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 34 in the sequence of Figure 196 (SEQ ID NO:278). The transmembrane domain has been tentatively identified as extending from about amino acid position 428 through about amino acid position 450 in the PRO1309 amino acid sequence (Figure 196, SEQ ID NO:278).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 35 to about 522, inclusive of Figure 196 (SEQ ID NO:278), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1309 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1309 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1309 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 35 through 522 of Figure 196 (SEQ ID NO:278).

In another aspect, the invention concerns an isolated PRO1309 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 35 to about 522, inclusive of Figure 196 (SEQ ID NO:278).

In a further aspect, the invention concerns an isolated PRO1309 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 35 through 522 of Figure 196 (SEQ ID NO:278).

In yet another aspect, the invention concerns an isolated PRO1309 polypeptide, comprising the sequence of amino acid residues 35 to about 522, inclusive of Figure 196 (SEQ ID NO:278), or a fragment thereof sufficient to provide a binding site for an anti-PRO1309 antibody. Preferably, the PRO1309 fragment retains a qualitative biological activity of a native PRO1309 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1309 polypeptide having the sequence of amino acid residues from about 35 to about 522, inclusive of Figure 196 (SEQ ID NO:278), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1309 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1309 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1309 polypeptide, by contacting the native PRO1309 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1309 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

84. PRO1028

Applicants have identified a cDNA clone that encodes a secreted novel polypeptide, wherein the polypeptide is designated in the present application as "PRO1028".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1028 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1028 polypeptide having amino acid residues 1 through 197 of Figure 198 (SEQ ID NO:281), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally,

under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on June 9, 1998 with the ATCC as DNA59603-1419 which includes the nucleotide sequence encoding PRO1028.

In another embodiment, the invention provides isolated PRO1028 polypeptide. In particular, the invention provides isolated native sequence PRO1028 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 197 of Figure 198 (SEQ ID NO:281). Optionally, the PRO1028 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on June 9, 1998 with the ATCC as DNA59603-1419.

85. PRO1027

A cDNA clone (DNA59605-1418) has been identified, having a type II fibronectin collagen-binding domain that encodes a novel polypeptide, designated in the present application as "PRO1027."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1027 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1027 polypeptide having the sequence of amino acid residues from about 1 or 34 to about 77, inclusive of Figure 200 (SEQ ID NO:283), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-77, or in another embodiment, 34-77.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1027 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 31 or 130 and about 261, inclusive, of Figure 199 (SEQ ID NO:282). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203005 (DNA59605-1418), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203005 (DNA59605-1418).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 34 to about 77, inclusive of Figure 200 (SEQ ID NO:283), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1027 polypeptide having the sequence of amino acid residues from about 1 or 34 to about 77, inclusive of Figure 200 (SEQ ID NO:283), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 34 to about 77, inclusive of Figure 200 (SEQ ID NO:283), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1027 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1027 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 34 through 77 of Figure 200 (SEQ ID NO:283).

In another aspect, the invention concerns an isolated PRO1027 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 34 to about 77, inclusive of Figure 200 (SEQ ID NO:283).

In a further aspect, the invention concerns an isolated PRO1027 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 34 through 77 of Figure 200 (SEQ ID NO:283).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1027 polypeptide having the sequence of amino acid residues from about 1 or 34 to about 77, inclusive of Figure 200 (SEQ ID NO:283), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1027 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1027 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1027 polypeptide, by contacting the native PRO1027 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1027 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

86. PRO1107

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with PC-1, wherein the polypeptide is designated in the present application as "PRO1107".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1107 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1107 polypeptide having amino acid residues 1 through 477 of Figure 202 (SEQ ID NO:285), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO1107 polypeptide having amino acid residues about 23 through 477 of Figure 202 (SEQ ID NO:285) or amino acids about 1 or 23 through 428 ± 5 of Figure 202 (SEQ ID NO:285), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA59606-1471 vector deposited on June 9, 1998 with the ATCC, which includes the nucleotide sequence encoding PRO1107.

In another embodiment, the invention provides isolated PRO1107 polypeptide. In particular, the invention provides isolated native sequence PRO1107 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 477 of Figure 202 (SEQ ID NO:285). Additional embodiments of the present invention are directed to PRO1107 polypeptides comprising amino acids about 23 through 477 of Figure 202 (SEQ ID NO:285) or amino acids about 1 or 23 through 428 ± 5 of Figure 202 (SEQ ID NO:285). Optionally, the PRO1107 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA59606-1471 vector deposited with the ATCC on June 9, 1998.

87. PRO1140

Applicants have identified a cDNA clone, DNA59607-1497, that encodes a novel multi-span transmembrane polypeptide wherein the polypeptide is designated in the present application as "PRO1140".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1140 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1140 polypeptide having the sequence of amino acid residues from 1 to about 255, inclusive of Figure 204 (SEQ ID NO:287), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1140 polypeptide comprising DNA that hybridizes to the complement of the nucleic acid sequence having about residues 210 to about 974, inclusive of Figure 203 (SEQ ID NO:286). Preferably, hybridization occurs under

stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209946 (DNA59607-1497), which was deposited on June 9, 1998, or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209946 (DNA59607-1497).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 255, inclusive of Figure 204 (SEQ ID NO:287).

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1140 extracellular domain (ECD), with or without the initiating methionine, and its soluble variants (i.e. transmembrane domain(s) deleted or inactivated) or is complementary to such encoding nucleic acid molecule. Referring to the PRO1140 amino acid sequence (SEQ ID NO:287) shown in Figure 204, transmembrane domain regions have been tentatively identified as extending from about amino acid positions 101 to about 118, about 141 to about 161, and from about 172 to about 191.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 90% positives, and most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 255, inclusive of Figure 204 (SEQ ID NO:287).

Another embodiment is directed to fragments of a PRO1140 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1140 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1140 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 255 of Figure 204 (SEQ ID NO:287).

In another aspect, the invention concerns an isolated PRO1140 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to 255, inclusive of Figure 204 (SEQ ID NO:287).

In a further aspect, the invention concerns an isolated PRO1140 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, and most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 255 of Figure 204 (SEQ ID NO:287).

In another aspect, the invention concerns a PRO1140 extracellular domain comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to X of Figure 204 (SEQ ID NO:287), wherein X is any one of amino acid residues 96 to 105 of Figure 204 (SEQ ID NO:287).

In yet another aspect, the invention concerns an isolated PRO1140 polypeptide, comprising the sequence of amino acid residues 1 to about 255, inclusive of Figure 204 (SEQ ID NO:287), or a fragment thereof sufficient to provide a binding site for an anti-PRO1140 antibody. Preferably, the PRO1140 fragment retains a qualitative biological activity of a native PRO1140 polypeptide.

In another aspect, the present invention is directed to fragments of a PRO1140 polypeptide which are sufficiently long to provide an epitope against which an antibody may be generated.

88. **PRO1106**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with a peroxisomal calcium-dependent solute carrier, wherein the polypeptide is designated in the present application as "PRO1106".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1106 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1106 polypeptide having amino acid residues 1 through 469 of Figure 206 (SEQ ID NO:289), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA59609-1470 vector deposited on June 9, 1998 with the ATCC, which includes the nucleotide sequence encoding PRO1106.

In another embodiment, the invention provides isolated PRO1106 polypeptide. In particular, the invention provides isolated native sequence PRO1106 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 469 of Figure 206 (SEQ ID NO:289). Optionally, the PRO1106 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA59609-1470 vector deposited with the ATCC on June 9, 1998.

89. **PRO1291**

A cDNA clone (DNA59610-1556) has been identified, having homology to nucleic acid encoding butyrophilin that encodes a novel polypeptide, designated in the present application as "PRO1291".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1291 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1291 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 282, inclusive of Figure 208 (SEQ ID

NO:291), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1291 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 61 or about 145 and about 906, inclusive, of Figure 207 (SEQ ID NO:290). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209990 (DNA59610-1556) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209990 (DNA59610-1556).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 29 to about 282, inclusive of Figure 208 (SEQ ID NO:291), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1291 polypeptide having the sequence of amino acid residues from 1 or about 29 to about 282, inclusive of Figure 208 (SEQ ID NO:291), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1291 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 28 in the sequence of Figure 208 (SEQ ID NO:291). The transmembrane domain has been tentatively identified as extending from about amino acid position 258 to about amino acid position 281 in the PRO1291 amino acid sequence (Figure 208, SEQ ID NO:291).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 282, inclusive of Figure 208 (SEQ ID NO:291), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1291 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,

preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 207 (SEQ ID NO:290).

In another embodiment, the invention provides isolated PRO1291 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1291 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 29 to about 282 of Figure 208 (SEQ ID NO:291).

In another aspect, the invention concerns an isolated PRO1291 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 29 to about 282, inclusive of Figure 208 (SEQ ID NO:291).

In a further aspect, the invention concerns an isolated PRO1291 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 282, inclusive of Figure 208 (SEQ ID NO:291).

In yet another aspect, the invention concerns an isolated PRO1291 polypeptide, comprising the sequence of amino acid residues 1 or about 29 to about 282, inclusive of Figure 208 (SEQ ID NO:291), or a fragment thereof sufficient to provide a binding site for an anti-PRO1291 antibody. Preferably, the PRO1291 fragment retains a qualitative biological activity of a native PRO1291 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1291 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 282, inclusive of Figure 208 (SEQ ID NO:291), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1291 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1291 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1291 polypeptide by contacting the native PRO1291 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1291 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

90. PRO1105

Applicants have identified a cDNA clone that encodes a novel polypeptide having two transmembrane domains, wherein the polypeptide is designated in the present application as "PRO1105".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1105 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1105 polypeptide having amino acid residues 1 through 180 of Figure 210 (SEQ ID NO:293), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO1105 polypeptide having amino acid residues about 20 through 180 of Figure 210 (SEQ ID NO:293), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA59612-1466 vector deposited on June 9, 1998 with the ATCC, which includes the nucleotide sequence encoding PRO1105.

In another embodiment, the invention provides isolated PRO1105 polypeptide. In particular, the invention provides isolated native sequence PRO1105 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 180 of Figure 210 (SEQ ID NO:293). Additional embodiments of the present invention are directed to PRO1105 polypeptides comprising amino acids about 20 through 180 of Figure 210 (SEQ ID NO:293). Other embodiments of the present invention are directed to PRO1105 polypeptides comprising amino acids about 1 through 79 and 100 through about 144 of Figure 210 (SEQ ID NO:293). Optionally, the PRO1105 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA59612-1466 vector deposited with the ATCC on June 9, 1998.

91. PRO511

A cDNA clone (DNA59613-1417) has been identified, having some sequence identity with RoBo-1 and phospholipase inhibitors that encodes a novel polypeptide, designated in the present application as "PRO1026."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1026 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1026 polypeptide having the sequence of amino acid residues from about 1 or 26 to about 237, inclusive of Figure 212 (SEQ ID NO:295), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-237, or in another embodiment, 26-237.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1026 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 233 or 308 and about 943, inclusive, of Figure 212 (SEQ ID NO:295). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203007 (DNA59613-1417), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203007 (DNA59613-1417).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 26 to about 237, inclusive of Figure 212 (SEQ ID NO:295), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1026 polypeptide having the sequence of amino acid residues from about 1 or 26 to about 237, inclusive of Figure 212 (SEQ ID NO:295), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 26 to about 237, inclusive of Figure 212 (SEQ ID NO:295), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1026 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1026 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 26 through 237 of Figure 212 (SEQ ID NO:295).

In another aspect, the invention concerns an isolated PRO1026 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 26 to about 237, inclusive of Figure 212 (SEQ ID NO:295).

In a further aspect, the invention concerns an isolated PRO1026 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 26 through 237 of Figure 212 (SEQ ID NO:295).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1026 polypeptide having the sequence of amino acid residues from about 1 or 26 to about 237, inclusive of Figure 212 (SEQ ID NO:295), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1026 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1026 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1026 polypeptide, by contacting the native PRO1026 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1026 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

92. **PRO1104**

A cDNA clone (DNA59616-1465) has been identified, that encodes a novel polypeptide, designated in the present application as "PRO1104."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1104 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1104 polypeptide having the sequence of amino acid residues from about 1 or about 23 to about 341, inclusive of Figure 214 (SEQ ID NO:297), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-341, or in another embodiment, 23-341.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1104 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 109 or 175 and about 1131, inclusive, of Figure 213 (SEQ ID NO:296). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209991 (DNA59616-1465), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC

Deposit No. 209991 (DNA59616-1465).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or about 23 to about 341, inclusive of Figure 214 (SEQ ID NO:297), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1104 polypeptide having the sequence of amino acid residues from about 1 or about 23 to about 341, inclusive of Figure 214 (SEQ ID NO:297), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 23 to about 341, inclusive of Figure 214 (SEQ ID NO:297), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1104 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1104 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 23 through 341 of Figure 214 (SEQ ID NO:297).

In another aspect, the invention concerns an isolated PRO1104 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 23 through about 341, inclusive of Figure 214 (SEQ ID NO:297).

In a further aspect, the invention concerns an isolated PRO1104 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 23 through 341 of Figure 214 (SEQ ID NO:297).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1104 polypeptide having the sequence of amino acid residues from about 1 or about 23 to about 341, inclusive of Figure 214 (SEQ ID NO:297), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii)

recovering the polypeptide from the cell culture.

93. **PRO1100**

A cDNA clone (DNA59619-1464) has been identified that encodes a novel polypeptide having multiple transmembrane domains, designated in the present application as "PRO1100."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1100 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1100 polypeptide having the sequence of amino acid residues from about 1 or 21 to about 320, inclusive of Figure 216 (SEQ ID NO:299), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-320, or in another embodiment, 21-320.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1100 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 33 or 93 and about 992, inclusive, of Figure 215 (SEQ ID NO:298). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203041 (DNA59619-1464), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203041 (DNA59619-1464).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 21 to about 320, inclusive of Figure 216 (SEQ ID NO:299), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1100 polypeptide having the sequence of amino acid residues from about 1 or 21 to about 320, inclusive of Figure 216 (SEQ ID NO:299), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1100 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 21 to about 320, inclusive of Figure 216 (SEQ ID NO:299), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1100 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1100 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 21 through 320 of Figure 216 (SEQ ID NO:299).

In another aspect, the invention concerns an isolated PRO1100 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 21 to about 320, inclusive of Figure 216 (SEQ ID NO:299).

In a further aspect, the invention concerns an isolated PRO1100 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 21 through 320 of Figure 216 (SEQ ID NO:299).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1100 polypeptide having the sequence of amino acid residues from about 1 or 21 to about 320, inclusive of Figure 216 (SEQ ID NO:299), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1100 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1100 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1100 polypeptide, by contacting the native PRO1100 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1100 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

94. PRO836

A cDNA clone (DNA59620-1463) has been identified, having some sequence identity with SLS1 that encodes a novel polypeptide, designated in the present application as "PRO836."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO836 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO836 polypeptide having the sequence of amino acid residues from about 1 or 30 to about 461, inclusive of Figure 218 (SEQ ID NO:301), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-461, or in another embodiment, 30-461.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO836 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 65 or 152 and about 1447, inclusive, of Figure 217 (SEQ ID NO:300). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209989 (DNA59620-1463), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209989 (DNA59620-1463).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 30 to about 461, inclusive of Figure 218 (SEQ ID NO:301), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO836 polypeptide having the sequence of amino acid residues from about 1 or 30 to about 461, inclusive of Figure 218 (SEQ ID NO:301), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the

amino acid sequence of residues 1 or 30 to about 461, inclusive of Figure 218 (SEQ ID NO:301), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO836 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO836 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 30 through 461 of Figure 218 (SEQ ID NO:301).

In another aspect, the invention concerns an isolated PRO836 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 30 to about 461, inclusive of Figure 218 (SEQ ID NO:301).

In a further aspect, the invention concerns an isolated PRO836 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 30 through 461 of Figure 218 (SEQ ID NO:301).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO836 polypeptide having the sequence of amino acid residues from about 1 or 30 to about 461, inclusive of Figure 218 (SEQ ID NO:301), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO836 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO836 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO836 polypeptide, by contacting the native PRO836 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO836 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

95. **PRO1141**

A cDNA clone (DNA59625-1498) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1141".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1141 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most

preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1141 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 247, inclusive of Figure 220 (SEQ ID NO:303), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1141 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 204 or about 261 and about 944, inclusive, of Figure 219 (SEQ ID NO:302). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209992 (DNA59625-1498) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209992 (DNA59625-1498).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 20 to about 247, inclusive of Figure 220 (SEQ ID NO:303), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1141 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 247, inclusive of Figure 220 (SEQ ID NO:303), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1141 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 19 in the sequence of Figure 220 (SEQ ID NO:303). The transmembrane domains have been tentatively identified as extending from about amino acid position 38 to about amino acid position 57, from about amino acid position 67 to about amino acid position 83, from about amino acid position 117 to about amino acid position 139 and from about amino acid position 153 to about amino acid position 170, in the PRO1141 amino acid sequence (Figure 220, SEQ ID NO:303).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the

amino acid sequence of residues 1 or about 20 to about 247, inclusive of Figure 220 (SEQ ID NO:303), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1141 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 219 (SEQ ID NO:302).

In another embodiment, the invention provides isolated PRO1141 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1141 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 20 to about 247 of Figure 220 (SEQ ID NO:303).

In another aspect, the invention concerns an isolated PRO1141 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 20 to about 247, inclusive of Figure 220 (SEQ ID NO:303).

In a further aspect, the invention concerns an isolated PRO1141 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 20 to about 247, inclusive of Figure 220 (SEQ ID NO:303).

In yet another aspect, the invention concerns an isolated PRO1141 polypeptide, comprising the sequence of amino acid residues 1 or about 20 to about 247, inclusive of Figure 220 (SEQ ID NO:303), or a fragment thereof sufficient to provide a binding site for an anti-PRO1141 antibody. Preferably, the PRO1141 fragment retains a qualitative biological activity of a native PRO1141 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1141 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 247, inclusive of Figure 220 (SEQ ID NO:303), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA33128 comprising the nucleotide sequence of SEQ ID NO:304 (see Figure 221).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA34256 comprising the nucleotide sequence of SEQ ID NO:305 (see Figure 222).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA47941 comprising the nucleotide sequence of SEQ ID NO:306 (see Figure 223).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA54389 comprising the nucleotide sequence of SEQ ID NO:307 (see Figure 224).

96. PRO1132

A cDNA clone (DNA59767-1489) has been identified that encodes a novel polypeptide having sequence identity with serine proteases and trypsinogen and designated in the present application as "PRO1132."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1132 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1132 polypeptide having the sequence of amino acid residues from about 23 to about 293, inclusive of Figure 226 (SEQ ID NO:309), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1132 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 420 and about 1232, inclusive, of Figure 225 (SEQ ID NO:308). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203108 (DNA59767-1489), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203108 (DNA59767-1489).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 23 to about 293, inclusive of Figure 226 (SEQ ID NO:309), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1132 polypeptide having the sequence of amino acid residues from about 23 to about 293, inclusive of Figure 226 (SEQ ID NO:309), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more

preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 23 to about 293, inclusive of Figure 226 (SEQ ID NO:309), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1132 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1132 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1132 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 23 through 293 of Figure 226 (SEQ ID NO:309).

In another aspect, the invention concerns an isolated PRO1132 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 23 to about 293, inclusive of Figure 226 (SEQ ID NO:309).

In a further aspect, the invention concerns an isolated PRO1132 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 23 through 293 of Figure 226 (SEQ ID NO:309).

In yet another aspect, the invention concerns an isolated PRO1132 polypeptide, comprising the sequence of amino acid residues 23 to about 293, inclusive of Figure 226 (SEQ ID NO:309), or a fragment thereof sufficient to provide a binding site for an anti-PRO1132 antibody. Preferably, the PRO1132 fragment retains a qualitative biological activity of a native PRO1132 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1132 polypeptide having the sequence of amino acid residues from about 23 to about 293, inclusive of Figure 226 (SEQ ID NO:309), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1132 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1132 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1132 polypeptide, by contacting the native PRO1132 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1132 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

97. PRO1346

A cDNA clone (DNA59776-1600) has been identified, that encodes a novel polypeptide, designated in the present application as PRO1346 (or NL7), having homology to known TIE ligands.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding an NL7 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding an NL7 polypeptide having the sequence of amino acid residues from about 51 to about 461, inclusive of Figure 228 (SEQ ID NO:314), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding an NL7 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 1-3 (ATG) and about 1381-1383 (CGC, preceding the TAG stop codon), inclusive, of Figure 227 (SEQ ID NO:313). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203128 (DNA59776-1600), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203128 (DNA59776-1600).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 51 to about 461, inclusive of Figure 228 (SEQ ID NO:314), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 1000 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding an NL7 polypeptide having the sequence of amino acid residues from about 51 to about 461, inclusive of Figure 228 (SEQ ID NO:314), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding an NL7 polypeptide, with or without the initiating methionine, or its soluble forms, i.e. transmembrane domain

deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domain has been tentatively identified as extending from about amino acid position 31 to about amino acid position 50 in the NL7 amino acid sequence (Figure 228, SEQ ID NO:314).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 51 to about 461, inclusive of Figure 228 (SEQ ID NO:314), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule, at least about 200 bases in length, which encodes a fragment of a native NL7 polypeptide.

In another embodiment, the invention provides an isolated NL7 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides an isolated native sequence NL7 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues from about 51 to about 461 of Figure 228 (SEQ ID NO:314).

In another aspect, the invention concerns an isolated NL7 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 51 to about 461, inclusive of Figure 228 (SEQ ID NO:314).

In a further aspect, the invention concerns an isolated NL7 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 51 to 461 of Figure 228 (SEQ ID NO:314).

In yet another aspect, the invention concerns an isolated NL7 polypeptide, comprising the sequence of amino acid residues from about 51 to about 461, inclusive of Figure 228 (SEQ ID NO:314), or a fragment thereof sufficient to provide a binding site for an anti-NL7 antibody. Preferably, the NL7 fragment retains a qualitative biological activity of a native NL7 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding an NL7 polypeptide having the sequence of amino acid residues from about 51 to about 461, inclusive of Figure 228 (SEQ ID NO:314), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native NL7 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-NL7 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native NL7 polypeptide, by contacting the native NL7 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising an NL7 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

98. **PRO1131**

A cDNA clone (DNA59777-1480) has been identified that encodes a novel polypeptide having sequence identity with LDL receptors and designated in the present application as "PRO1131."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1131 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1131 polypeptide having the sequence of amino acid residues from about 1 to about 280, inclusive of Figure 230 (SEQ ID NO:319), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1131 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 144 and about 983, inclusive, of Figure 229 (SEQ ID NO:318). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203111 (DNA59777-1480), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203111 (DNA59777-1480).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 280, inclusive of Figure 230 (SEQ ID NO:319), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1131 polypeptide having the sequence of amino acid residues from about 1 to about 280, inclusive of Figure 230 (SEQ ID NO:319), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most

preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1131 polypeptide in its soluble form, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domain (type II) has been tentatively identified as extending from about amino acid positions 49-74 in the amino acid sequence of Figure 230, SEQ ID NO:319.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 280, inclusive of Figure 230 (SEQ ID NO:319), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1131 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1131 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1131 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 280 of Figure 230 (SEQ ID NO:319).

In another aspect, the invention concerns an isolated PRO1131 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 280, inclusive of Figure 230 (SEQ ID NO:319).

In a further aspect, the invention concerns an isolated PRO1131 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 through 280 of Figure 230 (SEQ ID NO:319).

In yet another aspect, the invention concerns an isolated PRO1131 polypeptide, comprising the sequence of amino acid residues 1 to about 280, inclusive of Figure 230 (SEQ ID NO:319), or a fragment thereof sufficient to provide a binding site for an anti-PRO1131 antibody. Preferably, the PRO1131 fragment retains a qualitative biological activity of a native PRO1131 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1131 polypeptide having the sequence of amino acid residues from about 1 to about 280, inclusive of Figure 230 (SEQ ID NO:319), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising

the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1131 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1131 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1131 polypeptide, by contacting the native PRO1131 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1131 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA43546 comprising the nucleotide sequence of Figure 231 (SEQ ID NO:320).

99. **PRO1281**

A cDNA clone (DNA59820-1549) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1281".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1281 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1281 polypeptide having the sequence of amino acid residues from about 16 to about 775, inclusive of Figure 233 (SEQ ID NO:326), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1281 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 273 and about 2552, inclusive, of Figure 232 (SEQ ID NO:325). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203129 (DNA59820-1549), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203129 (DNA59820-1549).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 16 to about 775, inclusive of Figure 233 (SEQ ID NO:326), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1281 polypeptide having the sequence of amino acid residues from about 16 to about 775, inclusive of Figure 233 (SEQ ID NO:326), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1281 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 15 in the sequence of Figure 233 (SEQ ID NO:326).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to about 775, inclusive of Figure 233 (SEQ ID NO:326), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1281 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1281 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1281 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 16 to 775 of Figure 233 (SEQ ID NO:326).

In another aspect, the invention concerns an isolated PRO1281 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 16 to about 775, inclusive of Figure 233 (SEQ ID NO:326).

In a further aspect, the invention concerns an isolated PRO1281 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to 775 of Figure 233 (SEQ ID NO:326).

In yet another aspect, the invention concerns an isolated PRO1281 polypeptide, comprising the sequence of amino acid residues 16 to about 775, inclusive of Figure 233 (SEQ ID NO:326), or a fragment thereof sufficient to provide a binding site for an anti-PRO1281 antibody. Preferably, the PRO1281 fragment retains a qualitative biological activity of a native PRO1281 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1281 polypeptide having the sequence of amino acid residues from about 16 to about 775, inclusive of Figure 233 (SEQ ID NO:326), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

100. **PRO1064**

A cDNA clone (DNA59827-1426) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1064".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1064 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1064 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 153, inclusive of Figure 235 (SEQ ID NO:334), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1064 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 532 or about 604 and about 990, inclusive, of Figure 234 (SEQ ID NO:333). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203089 (DNA59827-1426) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203089 (DNA59827-1426).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 153, inclusive of Figure 235 (SEQ ID NO:334), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1064 polypeptide having the sequence of amino acid residues from 1 or about 25 to

about 153, inclusive of Figure 235 (SEQ ID NO:334), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1064 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 24 in the sequence of Figure 235 (SEQ ID NO:334). The transmembrane domain has been tentatively identified as extending from about amino acid position 89 to about amino acid position 110 in the PRO1064 amino acid sequence (Figure 235, SEQ ID NO:334).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 153, inclusive of Figure 235 (SEQ ID NO:334), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1064 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 234 (SEQ ID NO:333).

In another embodiment, the invention provides isolated PRO1064 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1064 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 25 to about 153 of Figure 235 (SEQ ID NO:334).

In another aspect, the invention concerns an isolated PRO1064 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 153, inclusive of Figure 235 (SEQ ID NO:334).

In a further aspect, the invention concerns an isolated PRO1064 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 153, inclusive of Figure 235 (SEQ ID NO:334).

In yet another aspect, the invention concerns an isolated PRO1064 polypeptide, comprising the sequence of amino acid residues 1 or about 25 to about 153, inclusive of Figure 235 (SEQ ID NO:334), or a fragment thereof sufficient to provide a binding site for an anti-PRO1064 antibody. Preferably, the PRO1064 fragment retains a qualitative biological activity of a native PRO1064 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1064 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 153, inclusive of Figure 235 (SEQ ID NO:334), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA45288 comprising the nucleotide sequence of SEQ ID NO:335 (see Figure 236).

101. PRO1379

A cDNA clone (DNA59828-1608) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1379."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1379 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1379 polypeptide having the sequence of amino acid residues from about 18 to about 574, inclusive of Figure 238 (SEQ ID NO:340), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1379 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 61 and about 1731, inclusive, of Figure 237 (SEQ ID NO:339). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203158 (DNA59828-1608), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203158 (DNA59828-1608).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 18 to about 574, inclusive of Figure 238 (SEQ ID NO:340), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1379 polypeptide having the sequence of amino acid residues from about 18 to about 574, inclusive of Figure 238 (SEQ ID NO:340), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1379 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 17 in the sequence of Figure 238 (SEQ ID NO:340).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to about 574, inclusive of Figure 238 (SEQ ID NO:340), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1379 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1379 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1379 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 18 to 574 of Figure 238 (SEQ ID NO:340).

In another aspect, the invention concerns an isolated PRO1379 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 18 to about 574, inclusive of Figure 238 (SEQ ID NO:340).

In a further aspect, the invention concerns an isolated PRO1379 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to 574 of Figure 238 (SEQ ID NO:340).

In yet another aspect, the invention concerns an isolated PRO1379 polypeptide, comprising the sequence of amino acid residues 18 to about 574, inclusive of Figure 238 (SEQ ID NO:340), or a fragment thereof sufficient to provide a binding site for an anti-PRO1379 antibody. Preferably, the PRO1379 fragment retains a qualitative biological activity of a native PRO1379 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1379 polypeptide having the sequence of amino acid residues from about 18 to about 574, inclusive of Figure 238 (SEQ ID NO:340), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

102. PRO844

A cDNA clone (DNA59838-1462) has been identified, having sequence identity with protease inhibitors, that encodes a novel polypeptide, designated in the present application as "PRO844."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO844 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO844 polypeptide having the sequence of amino acid residues from about 1 or 20 to about 111, inclusive of Figure 240 (SEQ ID NO:345), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-111, or in another embodiment, 20-111.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO844 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 5 or 62 and about 337, inclusive, of Figure 239 (SEQ ID NO:344). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209976 (DNA59838-1462), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209976 (DNA59838-1462).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 20 to about 111, inclusive of Figure 240 (SEQ ID NO:345), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO844 polypeptide having the sequence of amino acid residues from about 1 or 20 to about 111, inclusive of Figure 240 (SEQ ID NO:345), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 20 to about 111, inclusive of Figure 240 (SEQ ID NO:345), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO844 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO844 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 20 through 111 of Figure 240 (SEQ ID NO:345).

In another aspect, the invention concerns an isolated PRO844 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 20 to about 111, inclusive of Figure 240 (SEQ ID NO:345).

In a further aspect, the invention concerns an isolated PRO844 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 20 through 111 of Figure 240 (SEQ ID NO:345).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO844 polypeptide having the sequence of amino acid residues from about 1 or 20 to about 111, inclusive of Figure 240 (SEQ ID NO:345), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO844 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO844 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO844 polypeptide, by contacting the native PRO844 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO844 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

103. PRO848

A cDNA clone (DNA59839-1461) has been identified, having sequence identity with sialytransferases that encodes a novel polypeptide, designated in the present application as "PRO848."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO848 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO848 polypeptide having the sequence of amino acid residues from about 1 or 36 to about 600, inclusive of Figure 242 (SEQ ID NO:347), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-600, or in another embodiment, 36-600.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO848 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 1 or 251 and about 1945, inclusive, of Figure 241 (SEQ ID NO:346). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209988 (DNA59839-1461), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209988 (DNA59839-1461).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 36 to about 600, inclusive of Figure 242 (SEQ ID NO:347), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO848 polypeptide having the sequence of amino acid residues from about 1 or 36 to about 600, inclusive of Figure 242 (SEQ ID NO:347), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 36 to about 600, inclusive of Figure 242 (SEQ ID NO:347), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO848 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO848 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 36 through 600 of Figure 242 (SEQ ID NO:347).

In another aspect, the invention concerns an isolated PRO848 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 36 to about 600, inclusive of Figure 242 (SEQ ID NO:347).

In a further aspect, the invention concerns an isolated PRO848 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 36 through 600 of Figure 242 (SEQ ID NO:347).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO848 polypeptide having the sequence of amino acid residues from about 1 or 36 to about 600, inclusive of Figure 242 (SEQ ID NO:347), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO848 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO848 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO848 polypeptide, by contacting the native PRO848 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO848 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

104. PRO1097

Applicants have identified a cDNA clone (DNA59841-1460) that encodes a novel secreted polypeptide having domains therein from the glycoprotease family proteins and the acyltransferase ChoActase/COT/CPT family, wherein the polypeptide is designated in the present application as "PRO1097".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1097 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1097 polypeptide having the sequence of amino acid residues from about 1 or 21 to about 91, inclusive of Figure 244 (SEQ ID NO:349), or (b) the complement of the DNA molecule of (a). The term "or" as used herein to refer to amino or nucleic acids is meant to refer to two alternative embodiments provided herein, i.e., 1-91, or in another embodiment, 21-91.

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1097 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 3 or 63 and about 275, inclusive, of Figure 243 (SEQ ID NO:348). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203044 (DNA59841-1460), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203044 (DNA59841-1460).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 or 21 to about 91, inclusive of Figure 244 (SEQ ID NO:349), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1097 polypeptide having the sequence of amino acid residues from about 1 or 21 to about 91, inclusive of Figure 244 (SEQ ID NO:349), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1097 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 244 (SEQ ID NO:349).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more

preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 21 to about 91, inclusive of Figure 244 (SEQ ID NO:349), or (b) the complement of the DNA of (a).

In another embodiment, the invention provides isolated PRO1097 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1097 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 21 through 91 of Figure 244 (SEQ ID NO:349).

In another aspect, the invention concerns an isolated PRO1097 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or 21 to about 91, inclusive of Figure 244 (SEQ ID NO:349).

In a further aspect, the invention concerns an isolated PRO1097 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or 21 through 91 of Figure 244 (SEQ ID NO:349).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1097 polypeptide having the sequence of amino acid residues from about 1 or 21 to about 91, inclusive of Figure 244 (SEQ ID NO:349), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO1097 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1097 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1097 polypeptide, by contacting the native PRO1097 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1097 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

105. PRO1153

A cDNA clone (DNA59842-1502) has been identified, having two transmembrane domains and being very proline rich, that encodes a novel polypeptide, designated in the present application as "PRO1153."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1153 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1153 polypeptide having the sequence of amino acid residues from about 1 to about 197, inclusive of Figure 246 (SEQ ID NO:351), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1153 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 92 and about 682, inclusive, of Figure 245 (SEQ ID NO:350). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209982 (DNA59842-1502), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209982 (DNA59842-1502).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 197, inclusive of Figure 246 (SEQ ID NO:351), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1153 polypeptide having the sequence of amino acid residues from about 1 to about 197, inclusive of Figure 246 (SEQ ID NO:351), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1153 polypeptide, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains have been tentatively identified as extending from about amino acid positions 10-28 and 85-110 in the PRO1153 amino acid sequence (Figure 246, SEQ ID NO:351).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 197, inclusive of Figure 246 (SEQ ID NO:351), or (b) the complement of the DNA of (a).